

# **1,2-Dibromo-3-chloropropane in Drinking-water**

Background document for development of  
WHO *Guidelines for Drinking-water Quality*

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## Preface

One of the primary goals of WHO and its member states is that “all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water.” A major WHO function to achieve such goals is the responsibility “to propose regulations, and to make recommendations with respect to international health matters ....”

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as International Standards for Drinking-Water. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO Guidelines for drinking-water quality (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A “final task force” meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health

Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues, and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.

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## GENERAL DESCRIPTION

### *Identity*

CAS no.: 96-12-8

Molecular formula: C<sub>3</sub>H<sub>5</sub>Br<sub>2</sub>Cl

**Physicochemical properties** (1) [Conversion factor in air: 1 ppm = 9.67 mg/m<sup>3</sup>]

<i>Property</i>	<i>Value</i>
Physical state	liquid
Boiling point	196 °C
Vapour pressure	0.1 kPa at 21 °C
Water solubility	1230 mg/litre
Log octanol–water partition coefficient	2.43

### *Organoleptic properties*

The odour and taste thresholds for 1,2-dibromo-3-chloropropane (DBCP) in water are both 0.01 mg/litre (1).

### *Major uses*

DBCP is used as a nematocidal fumigant (1).

### *Environmental fate*

DBCP is expected to volatilize from surface water. It is highly persistent in soil and has been shown to remain there for more than 2 years. It is mobile in soil and may migrate to groundwater (1).

## ANALYTICAL METHODS

DBCP is determined by a purge-and-trap gas chromatographic procedure used for the determination of volatile organohalides in drinking-water (2). This method is applicable to the measurement of DBCP over a concentration range of 0.03–1500 µg/litre. Confirmation is by mass spectrometry (detection limit 0.2 µg/litre). A detection limit of 0.02 µg/litre is possible when gas chromatography and electron-capture detection are used (3).

## ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

### *Air*

DBCP is a low-level contaminant in air (1).

### *Water*

In a survey of drinking-water wells near locations where DBCP had been used within the previous 2 years, this compound was found at low (µg/litre) levels. In wells not used for drinking-water, it has been detected at levels of up to 20 µg/litre (1).

### *Food*

DBCP has been identified as a contaminant in vegetables grown in soils treated with it (1).

## KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

On the basis of excretion studies, absorption is expected to be high by the oral route. Distribution is primarily to the liver and kidneys (4). Transplacental transfer also appears to occur (5).

Metabolic pathways for DBCP may involve epihalohydrin, other reactive epoxides, or 2-bromoacrolein as intermediates. Urinary metabolites in rats include mercapturic acid conjugates,  $\beta$ -chlorolactic acid,  $\beta$ -bromolactic acid, and 2-bromoacrylic acid (1). Most DBCP is excreted by the urinary and faecal routes; smaller amounts are excreted in expired air. The urine is the predominant route for the elimination of metabolites (6).

## EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

### *Acute exposure*

Acute oral LD<sub>50</sub>s of 170, 410, and 440 mg/kg of body weight were reported for rats, mice, and rabbits, respectively (1).

### *Short-term exposure*

Dietary administration of DBCP to rats for 90 days resulted in increased kidney weights at 2 mg/kg of body weight per day, reduced body weight gain at 15 mg/kg of body weight per day, increased liver weight at 45 mg/kg of body weight per day, and muscular weakness and increased mortality at 135 mg/kg of body weight per day. The NOAEL was 0.5 mg/kg of body weight per day (7).

In a study in which Sprague-Dawley rats were given DBCP in drinking-water at concentrations of 0, 5, 50, 100, or 200 mg/litre (approximately 0, 0.4, 3.2, 5.2, and 9.4 mg/kg of body weight) for 64 days, renal lesions, increased protein and glucose levels, and increased urinary specific gravity were apparent at the two highest doses (8).

### *Long-term exposure*

In a chronic study in which mice and rats received DBCP by gavage, a dose-related increase in mortality and a high incidence of toxic tubular nephropathy were reported at time-weighted average doses of 78.6–149.3 mg/kg of body weight per day in mice and 10.7 and 20.7 mg/kg of body weight per day in rats (9). Lifetime treatment of Charles River CD rats with doses of 0, 0.2, 0.68, or 2 mg/kg of body weight per day in the diet resulted in kidney lesions in female rats and reduced body weight and organ weight changes in male rats given 2 mg/kg of body weight per day (10).

### *Reproductive toxicity, embryotoxicity, and teratogenicity*

In a study in which male Dutch rabbits (6 per group) were given DBCP at 0, 0.9, 1.9, 3.7, 7.5, or 15 mg/kg of body weight in drinking-water 5 days per week for 10 weeks, testis weights and sperm production decreased and follicle stimulating hormone levels increased at 15 mg/kg of body weight, mean seminiferous tubular diameter decreased at 7.5 mg/kg of body weight, and abnormal sperm morphology was observed at 1.9 mg/kg of body weight. The NOAEL was 0.9 mg/kg of body weight (11,12).

In a study in which DBCP was administered at 0.02, 0.2, 2, or 20 mg/kg of body weight per day in drinking-water to male and female Sprague-Dawley rats for 60 days before mating, throughout mating, during gestation, and during the first 5 days of lactation, fetal body weights, pup weights, and food and water intake were reduced at the highest dose (13).

Administration of DBCP at 0, 25, 50, or 100 mg/kg of body weight by gavage in corn oil to male and female CD-1 mice during the premating period (7 days), cohabitation (98 days) and segregation (21 days) was without effect on reproduction in the F<sub>0</sub> generation; however, when treatment at 100 mg/kg of body weight was administered to the offspring of F<sub>1</sub> mice, organ weights were reduced (14).

Male Sprague-Dawley rats given DBCP in corn oil by gavage at doses of 0, 0.9, 1.9, 3.7, 7.5, or 15 mg/kg of body weight for 77 days and mated with untreated females on days 65–71 had decreased body and testis weights at 3.7 but not at 7.5 mg/kg of body weight. Daily spermatozoa production was significantly lower in vehicle controls than in controls not given corn oil (15).

No teratogenic effects were found in fetuses of pregnant Wistar rats treated with DBCP by gavage at 12.5, 25, or 50 mg/kg of body weight per day on days 6–15 of gestation (5). The dose of 50 mg/kg of body weight per day was fatal to embryos, and those of 25 and 50 mg/kg of body weight per day reduced maternal body weights.

### ***Mutagenicity and related end-points***

Technical-grade DBCP was mutagenic in *Salmonella typhimurium* strains TA1535, TA1530, TA100, and TA98 and in *Escherichia coli*, with and without metabolic activation (16–21). Results were negative with *S. typhimurium* strains A-98, TA1537, and TA1538 (16,19,20). DBCP was positive in the recessive lethal assay, in a genetic crossing-over assay, and for chromosome breakage in *Drosophila melanogaster* (22–24). Results of a dominant lethal assay were positive in rats (25) but negative in mice (26). Positive results were obtained in a study on sister chromatid exchange in cultured Chinese hamster cells, for chromosomal aberrations in rats treated *in vivo*, and for unscheduled DNA synthesis in germ cells of prepubertal mice treated *in vivo* (26–28). Results were negative in the mouse specific locus test (29).

### ***Carcinogenicity***

In a chronic study in which Osborne-Mendel rats received time-weighted average doses by gavage of 10.7 and 20.7 mg/kg of body weight per day, highly significant dose-related increased incidences of squamous cell carcinoma of the forestomach in males and females and mammary adenocarcinoma in females were observed. Significant dose-related increased incidences of squamous cell carcinoma of the forestomach of male and female B6C3F<sub>1</sub> mice were found at time-weighted average doses of 78.6–149.3 mg/kg of body weight per day (9).

In a chronic dietary carcinogenicity bioassay in Charles River rats, high-dose (2.0 mg/kg of body weight per day) male and female rats had significantly increased incidences of carcinoma of the renal tubules and squamous cell carcinoma of the stomach. Male rats also showed an increase in liver tumours following exposure to DBCP for 104 weeks (10).

In a chronic inhalation study, dose-related increased incidences of nasal cavity tumours were found in male and female F344 rats and B6C3F<sub>1</sub> mice at DBCP concentrations of 5.8 or 29 mg/m<sup>3</sup>, 6 h per day, 5 days per week. The mice also had treatment-related increased incidences of pulmonary tumours (30).

DBCP was positive as a tumour initiator in the skin of Han/ICR Swiss mice but negative as a whole carcinogen for skin (31).



## EFFECTS ON HUMANS

Reduced spermatogenesis, which was reversible, was reported in chemical plant workers and agricultural workers exposed to DBCP (1). Possible permanent destruction of germinal epithelium was reported in a follow-up of exposed workers (32). No chromosomal aberrations were identified in men in whom spermatogenesis was suppressed as a result of occupational exposure to DBCP, nor were there increases in abortions and malformations in offspring (33). Results were negative in an epidemiological study of the relationship between DBCP contamination of drinking-water and reproductive indices (e.g., birth rate, birth weight, birth defects) (34). Approximately 98% of 45 914 mothers were exposed to 3 µg/litre or less of DBCP.

No association was found between DBCP contamination of drinking-water (average levels 0.004–5.8 µg/litre) and incidences of gastric cancer and leukaemia (35); 14% of the areas concerned had levels greater than 1 µg/litre. These results differ from those of a similar earlier study that indicated a tentative association between DBCP exposure in drinking-water and gastric cancer and leukaemia (36). There was no association between cancer incidence and DBCP exposure in a cohort of 550 chemical workers potentially exposed to this compound during its production from 1957 to 1975 (37). Exposure levels were not estimated.

## GUIDELINE VALUE

On the basis of data from studies on different strains of rats and mice, DBCP was determined to be carcinogenic in both sexes by the oral, inhalation, and dermal routes. It was also determined to be a reproductive toxicant in humans and several species of laboratory animals. IARC has classified DBCP in Group 2B (possible human carcinogen) based upon sufficient evidence of carcinogenicity in animals (38). Recent epidemiological evidence suggests an increase in cancer mortality in individuals exposed to high levels of DBCP. It was found to be genotoxic in a majority of *in vitro* and *in vivo* assays.

The linearized multistage model was applied to the data on the incidence of stomach, kidney, and liver tumours in the male rat in a 104-week dietary study (10). The concentrations in drinking-water relating to excess lifetime cancer risks of  $10^{-4}$ ,  $10^{-5}$ , and  $10^{-6}$  are 10, 1, and 0.1 µg/litre, respectively. The guideline values associated with these excess lifetime cancer risks are therefore 10, 1, and 0.1 µg/litre, respectively. An adequate margin of safety exists at these concentrations for the reproductive toxicity of DBCP. For a contaminated water supply, extensive treatment (e.g., air stripping followed by adsorption to granular activated carbon) would be required to reduce the level of DBCP to the guideline values.

## REFERENCES

1. Office of Drinking Water. *Drinking water criteria document for 1,2-dibromo-3-chloropropane (DBCP)*. Washington, DC, US Environmental Protection Agency, 1988 (ECAO-CIN-410).
2. Environmental Monitoring and Support Laboratory. *Method 502.1. Volatile halogenated organic compounds in water by purge-and-trap gas chromatography*. Cincinnati, OH, US Environmental Protection Agency, 1985.
3. Environmental Monitoring and Support Laboratory. *Method 524.1. Volatile organic compounds in water by purge-and-trap gas chromatography/mass spectrometry*. Cincinnati, OH, US Environmental Protection Agency, 1985.
4. Kato Y et al. Metabolic fate of DBCP in rats. III. Correlation between macromolecular binding of DBCP-metabolite and pathogenicity of necrosis. *Journal of pesticide science*, 1980, 5(1):81-88.

5. Ruddick JA, Newsome WH. A teratogenicity and tissue distribution study on dibromochloropropane in the rat. *Bulletin of environmental contamination and toxicology*, 1979, 21:483-487.
6. Kato Y et al. Metabolic fate of 1,2-dibromo-3-chloropropane (DBCP) in rats. *Journal of pesticide science*, 1979, 4:195-203.
7. Torkelson TR, Sadek SE, Rowe VK. Toxicologic investigations of 1,2-dibromo-3-chloropropane. *Toxicology and applied pharmacology*, 1961, 3:545-559.
8. Heindel JJ, Bruckner JV, Steinberger E. *A protocol for the determination of the no-effect level of 1,2-dibromo-3-chloropropane (DBCP) on the qualitative morphological integrity of the testicular seminiferous epithelium*. Washington, DC, US Environmental Protection Agency, Office of Drinking Water, 1983.
9. National Cancer Institute. *Bioassay of dibromochloropropane for possible carcinogenicity*. Bethesda, MD, 1977 (NCI Carcinogenesis Technical Report Serial No. 28; NTIS PB 277-472).
10. Hazleton Laboratories America, Inc. *104-week dietary study in rats, 1,2-dibromo-3-chloropropane (DBCP). Final report*. Midland, MI, Dow Chemical Co., 1977 (unpublished report, project no. 174-122).
11. Foote RH, Schermerhorn EC, Simkin ME. Measurement of semen quality, fertility and reproductive hormones to assess dibromochloropropane (DBCP) effects in live rabbits. *Fundamental and applied toxicology*, 1986, 6:628-637.
12. Foote RH, Berndtson WE, Rounsaville TR. Use of quantitative testicular histology to assess the effect of dibromochloropropane (DBCP) on reproduction in rabbits. *Fundamental and applied toxicology*, 1986, 6:638-647.
13. Johnston RV et al. Single-generation drinking water reproduction study of 1,2-dibromo-3-chloropropane in Sprague-Dawley rats. *Bulletin of environmental contamination and toxicology*, 1986, 37(4):531-537.
14. Reel JR et al. *Dibromochloropropane: reproduction and fertility assessment in CD-1 mice when administered by gavage*. Research Triangle Park, NC, US Department of Health and Human Services, National Toxicology Program, 1984 (NTP-84-263).
15. Amann RP, Berndtsen WE. Assessment of procedures for screening agents for effects on male reproduction. Effects of dibromochloropropane (DBCP) in the rat. *Fundamental and applied toxicology*, 1986, 7(2):244-255.
16. Rosenkranz HS. Genetic activity of 1,2-dibromo-3-chloropropane, a widely used fumigant. *Bulletin of environmental contamination and toxicology*, 1975, 14(1):8-12.
17. Prival MJ et al. Tris(2,3-dibromopropylphosphate): mutagenicity of a widely used flame retardant. *Science*, 1977, 195:76-78.
18. Stolzenberg SJ, Hine CH. Mutagenicity of halogenated and oxygenated three-carbon compounds. *Journal of toxicology and environmental health*, 1979, 5(6):1149-1158.
19. McKee RH, Phillips RD, Traul KA. The genetic toxicology of 1,2-dibromo-3-chloropropane, 1,2-dibromo-3-chloro-2-methylpropane, and 1,2,2-tribromo-2-methylpropane. *Cell biology and toxicology*, 1987, 3(4):391-406.
20. Ratpan F, Plaumann H. Mutagenicity of halogenated propanes and their methylated derivatives. *Environmental and molecular mutagenesis*, 1988, 12(2):253-259.
21. Ohta T et al. The SOS function-inducing activity of chemical mutagens in *Escherichia coli*. *Mutation research*, 1984, 131:101-109.
22. Kale PG, Baum JW. Genetic effects of 1,2-dibromo-3-chloropropane in *Drosophila*. *Environmental mutagenesis*, 1982, 4(6):681-688.
23. Inoue T et al. Induction of sex-linked recessive lethal mutations in *Drosophila melanogaster* males by gaseous 1,2-dibromo-3-chloropropane (DBCP). *Mutation research*, 1982, 105:89-94.
24. Zimmering S. 1,2-Dibromo-3-chloropropane (DBCP) is positive for sex-linked recessive lethals, heritable translocations and chromosome loss in *Drosophila*. *Mutation research*, 1983, 119(3):287-288.
25. Teramoto S et al. Dominant lethal mutation induced in male rats by 1,2-dibromo-3-chloropropane (DBCP). *Mutation research*, 1980, 77(1):71-78.

26. Lee IP, Suzuki K. Induction of unscheduled DNA synthesis in mouse germ cells following 1,2-dibromo-3-chloropropane (DBCP) exposure. *Mutation research*, 1979, 68:169-179.
27. Tezuka H et al. Sister-chromatid exchanges and chromosomal aberrations in cultured Chinese hamster cells treated with pesticides positive in microbial reversion assays. *Mutation research*, 1980, 78(2):177-191.
28. Whorton M, Foliat D. Mutagenicity, carcinogenicity and reproductive effects of dibromochloropropane (DBCP). *Mutation research*, 1983, 123:13-30.
29. Russell LB, Hunsicker PR, Cacheiro NLA. Mouse specific-locus test for the induction of heritable gene mutations by dibromochloropropane (DBCP). *Mutation research*, 1986, 170:161-166.
30. National Toxicology Program. *Carcinogenesis bioassay of 1,2-dibromo-3-chloropropane in F344 rats and B6C3F<sub>1</sub> mice (inhalation study)*. Research Triangle Park, NC, US Department of Health and Human Services, 1982 (NTP Technical Report No. 81-21; DHHS [NIH] 82-1762).
31. Van Duuren BL et al. Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. *Journal of the National Cancer Institute*, 1979, 63(6):1433-1439.
32. Eaton M et al. Seven-year follow-up of workers exposed to 1,2-dibromo-3-chloropropane. *Journal of occupational medicine*, 1986, 28:1145-1150.
33. Potashnik G, Abeliovich D. Chromosomal analysis and health status of children conceived to men during or following dibromochloropropane-induced spermatogenic suppression. *Andrologia*, 1985, 17:291-296.
34. Environmental Health Associates, Inc. *An epidemiologic investigation of the relationship between DBCP contamination in drinking water and reproductive effects in Fresno County, CA*. Houston, TX, Shell Oil Company, 1986 (unpublished report).
35. Environmental Health Associates, Inc. *Final report: examination of the possible relationship between DBCP water contamination and leukemia and gastric cancer in Fresno County, CA*. Houston, TX, Shell Oil Company, 1986 (unpublished report).
36. Jackson RJ et al. *Literature review on the toxicological aspects of DBCP and an epidemiological comparison of patterns of DBCP drinking water contamination with mortality rates from selected cancers in Fresno County, CA, 1970-1979*. California Department of Health Services, 1982 (unpublished report).
37. Hearn S et al. Mortality experience of employees with occupational exposure to DBCP. *Archives of environmental health*, 1984, 39:49-55.
38. International Agency for Research on Cancer. *Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1-42*. Lyon, 1987:191-192 (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Suppl. 7).