

Dichloromethane 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.: 75-09-2

Molecular formula: CH₂Cl₂

Dichloromethane is also known as methylene chloride.

Physicochemical properties (1,2) [Conversion factor in air: 1 ppm = 3.53 mg/m³]

<i>Property</i>	<i>Value</i>
Melting point	-95.1 °C
Boiling point	40 °C
Density	1.3255 g/cm ³ at 20 °C
Vapour pressure	46.53 kPa at 20 °C
Water solubility	20 000 mg/litre at 20 °C
Log octanol–water partition coefficient	1.3

Organoleptic properties

The odour thresholds for dichloromethane in air and water are 530–2120 mg/m³ and 9.1 mg/liter, respectively (3,4).

Major uses

Dichloromethane is widely used as an organic solvent and is found in paints, insecticides, degreasing and cleaning fluids, and other products (2,5,6).

Environmental fate

Most dichloromethane released to water and soil will be vaporized. It can persist in air for up to 500 days, but is rapidly biodegraded in water. In soil, it undergoes only slight biodegradation and is highly mobile, being leached from subsurface soil into groundwater (5,6).

ANALYTICAL METHODS

Purge-and-trap gas chromatography is routinely used for the determination of dichloromethane and other volatile organohalides in drinking-water (7). This method is suitable for use at concentrations of 1–1500 µg/litre, but there are difficulties at low concentrations because dichloromethane vapour readily penetrates tubing during the procedure. Mass spectrometry (detection limit 0.3 µg/litre) can be used to confirm the identity of the compound (8).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

Background levels in air are usually about 0.1 mg/m³; average concentrations in urban air range between 1 and 7 µg/m³ (2).

Water

Dichloromethane has been found in surface water samples at concentrations ranging from 0.1 to 743 µg/litre. Levels are usually higher in groundwater because volatilization is restricted;

concentrations as high as 3600 µg/litre have been reported (5). Mean concentrations in drinking-water were less than 1 µg/litre.

Food

Food is not expected to be a significant source of exposure to dichloromethane, which is now rarely used in food-extraction processes (e.g. decaffeination of coffee); however, it is used as a post-harvest fumigant on some foods (e.g. strawberries and grains).

Estimated total exposure and relative contribution of drinking-water

Inhalation is the major route of environmental exposure (2), the estimated average daily intake from urban air being 33–307 µg (5). Exposure to dichloromethane through food and drinking-water is insignificant.

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Dichloromethane appears to be readily absorbed from the gastrointestinal tract (2,9). Distribution in rats after oral administration was primarily to liver (10). The cytochrome P-450 and glutathione *S*-transferase systems can both metabolize dichloromethane to carbon monoxide or carbon dioxide (5,11). Animal data indicate that dichloromethane is excreted primarily through the lungs, the excretion products depending on the dose (10).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Dichloromethane has a low acute toxicity; LD₅₀ values of 2000 mg/kg of body weight for rats and mice have been reported (2,12,13). The primary effect associated with acute exposure is depression of the central nervous system.

Short-term exposure

Fischer 344 rats (20 per sex per group) were given dichloromethane in drinking-water for 90 days (0, 166, 420, or 1200 mg/kg of body weight per day in males, and 0, 209, 607, or 1469 mg/kg of body weight per day in females) (14). Centrilobular necrosis and granulomatous foci were noted in mid- and high-dose animals, and changes in some clinical chemistry parameters were noted in mid- and high-dose females. An increased incidence of hepatocyte vacuolization (lipid accumulation) was found in all dose groups. The LOAELs were 166 and 209 mg/kg of body weight per day for male and female rats, respectively.

In a study in which B6C3F₁ mice (20 per sex per group) received dichloromethane in drinking-water for 90 days at doses of 0, 226, 587, or 1911 mg/kg of body weight per day (males) and 0, 231, 586, or 2030 mg/kg of body weight per day (females), subtle centrilobular fatty changes in liver and slight decreases in body weight were seen in the mid- and high-dose groups. The NOAELs were 226 and 231 mg/kg of body weight per day for male and female mice, respectively (14).

Dichloromethane administered to Wistar rats in drinking-water at 125 mg/litre (17.5 mg/kg of body weight per day) (15) for 13 weeks did not affect behaviour, body weight, blood and urine chemistries, organ-to-body-weight ratios, or histopathology, except that the urine albumin test was often positive (2,16).

Long-term exposure

Fischer 344 rats (85 per sex per group) received estimated mean doses of 6, 52, 125, or 235 mg/kg of body weight per day (males) and 6, 58, 136, or 263 mg/kg of body weight per day (females) for 104 weeks (17). Hepatic histological alterations (including an increased incidence of foci/areas of cellular alterations and fatty changes) were detected at 52 mg/kg of body weight per day and above. There were no other treatment-related effects (e.g. on survival, organ weight, gross pathology) at any dose tested. The NOAEL for hepatic effects was 6 mg/kg of body weight per day.

When given to B6C3F₁ mice for 104 weeks at estimated mean doses of 0, 61, 124, 177, or 234 mg/kg of body weight per day for males (100–200 per dose) and 0, 59, 118, 172, or 238 mg/kg of body weight per day for females (50–100 per dose), dichloromethane did not affect body weight, water consumption, survival, clinical signs, haematological parameters, or gross pathology in any dose group. The histological alterations seen consisted of increased Oil Red O-positive material in both sexes at the highest dose tested. A NOAEL of 175 mg/kg of body weight per day (average for males and females) was identified (18).

Reproductive toxicity, embryotoxicity, and teratogenicity

In a two-generation study in which Fischer 344 rats were exposed to dichloromethane via inhalation at levels up to 5.3 g/m³, no effects on fertility, litter size, neonatal growth and survival, or histopathology were observed (19). In a study in which mice and rats were exposed to dichloromethane at 4.4 or 15.9 g/m³ during gestation (2,20,21), fetal body weights were reduced in rats at 15.9 g/m³ (21), and minor skeletal variants (e.g. decreased incidence of lumbar spur in rats and increased incidence of a single extra sternal ossification centre in mice) were found at 4.4 g/m³ (20).

Mutagenicity and related end-points

Dichloromethane was positive in the *Salmonella typhimurium* assay with and without activation (22). Test results in cultured mammalian cells are usually negative, but dichloromethane has been shown to transform rat embryo cells and to enhance the viral transformation of Syrian hamster embryo cells (23,24). No DNA alkylation was detected in rats and mice after inhalation of dichloromethane (25).

Carcinogenicity

Fischer 344 rats (85 per sex per group) received estimated mean doses of 6, 52, 125, or 235 mg/kg of body weight per day (males) and 6, 58, 136, or 263 mg/kg of body weight per day (females) in drinking-water for 104 weeks (17). Although the incidence of combined hepatocellular carcinomas and neoplastic nodules increased significantly in females in the groups receiving doses of 58 and 263 mg/kg of body weight per day (4/83, 6/85) as compared with controls (0/134), the number of tumours was similar to that for historical controls. No significant increase in liver tumours was evident in any of the male dose groups. The dose of 235 mg/kg of body weight per day was concluded to be borderline for carcinogenicity in Fischer 344 rats (6).

B6C3F₁ mice received dichloromethane in drinking-water for 104 weeks at estimated mean doses of 0, 61, 124, 177, or 234 mg/kg of body weight per day (males) and 0, 59, 118, 172, or 238 mg/kg of body weight per day (females) (18). There was a marginal increase in the incidence of combined hepatocellular adenomas/carcinomas in male mice in the groups receiving doses of 124, 177 and 234 mg/kg of body weight per day (30/100, 31/99, 35/125) as compared with controls (24/125) but the incidence rates were within the historical control

range. Liver tumours were not observed in female mice. This study is regarded as providing suggestive but not conclusive evidence for the carcinogenicity of dichloromethane (6).

Groups of B6C3F₁ mice (50 per sex per dose) were exposed by inhalation to 0, 7.1 or 14.1 g/m³ dichloromethane for 102 weeks (26). The incidence of alveolar/bronchiolar carcinomas was increased in both dose groups in males (10/50, 28/50) and females (13/48, 29/48) as compared with controls (2/50 males, 1/50 females). The combined incidence of hepatocellular adenomas and hepatocellular carcinomas was increased in high-dose males (33/49 v. 22/50 and 24/49 for the control and low-dose group) and high-dose females (40/48 v. 3/50 and 16/48). This study was regarded as clear evidence of carcinogenicity in mice.

EFFECTS ON HUMANS

Inhalation of a high concentration of dichloromethane has been associated with a variety of central nervous system effects, most notably narcosis. Acute exposure to levels of 1.06 g/m³ in air can impair sensory and motor function (2,27). Epidemiological studies involving occupational exposure (2,28–31) have failed to show a positive correlation between inhalation exposure and increased cancer incidence.

GUIDELINE VALUE

Dichloromethane is of low acute toxicity. An inhalation study in mice provided conclusive evidence of carcinogenicity, whereas a drinking-water study provided only suggestive evidence. IARC has placed dichloromethane in group 2B (possible human carcinogen) (32); however, the evidence suggests that it is not a genotoxic carcinogen and that genotoxic metabolites are not formed in relevant amounts *in vivo*.

A TDI of 6 µg/kg of body weight was calculated by applying an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 reflecting concern for carcinogenic potential) to a NOAEL of 6 mg/kg of body weight per day for hepatotoxic effects in a 2-year drinking-water study in rats (17). This gives a guideline value of 20 µg/litre (rounded figure), based on the allocation of 10% of the TDI to drinking-water. It should be noted that widespread exposure from other sources is possible.

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