WHO/SDE/WSH/03.04/19
English only

1,1-Dichloroethane in Drinking-water

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

Originally published in **Guidelines for drinking-water quality,** 2nd ed. Vol.2**.** *Health criteria and other supporting information.* World Health Organization, Geneva, 1996.

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**.**

Acknowledgements

The work of the following coordinators was crucial in the development of this background document for development of WHO *Guidelines for drinking-water quality*:

J.K. Fawell, Water Research Centre, United Kingdom (inorganic constituents)
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The efforts of all who helped in the preparation and finalization of this document, including those who drafted and peer reviewed drafts, are gratefully acknowledged.

The convening of the experts meetings was made possible by the financial support afforded to WHO by the Danish International Development Agency (DANIDA), Norwegian Agency for Development Cooperation (NORAD), the United Kingdom Overseas Development Administration (ODA) and the Water Services Association in the United Kingdom, the Swedish International Development Authority (SIDA), and the following sponsoring countries: Belgium, Canada, France, Italy, Japan, Netherlands, United Kingdom of Great Britain and Northern Ireland and United States of America.

GENERAL DESCRIPTION

Identity

CAS no.: 75-34-3
Molecular formula: $C_2H_4Cl_2$

Physicochemical properties (*1,2*) [Conversion factor in air: 1 ppm = 4.05 mg/m^3]

Property	*Value*
Melting point	-97.4 °C
Boiling point	57.3 °C
Density	1.174 g/cm^3 at 20 °C
Vapour pressure	31.2 kPa at 20 °C
Water solubility	5500 mg/litre at 20 °C
Log octanol-water partition coefficient	61.7

Organoleptic properties

1,1-Dichloroethane has an aromatic, ethereal and chloroform-like odour. Its odour threshold in air is 486 or 810 mg/m^3 (*2*).

Major uses

The major use of 1,1-dichloroethane is as an intermediate in the production of 1,1,1-trichloroethane, vinyl chloride, and other chemicals (*3*). It is also used as a solvent in paint and varnish removers, as a degreaser and cleaning agent, and in ore flotation. It was formerly used as an anaesthetic.

Environmental fate

Most 1,1-dichloroethane released to the environment will be vaporized and enter the atmosphere, where photo-oxidation takes place; the estimated half-life is 44 days. Biodegradation is not expected to be significant in aquatic systems (*3*).

ANALYTICAL METHODS

A purge-and-trap gas chromatographic procedure is used for the determination of 1,1-dichloroethane and other volatile organohalides in drinking-water (*4*). This method is applicable to the measurement of 1,1-dichloroethane over a concentration range of 0.02–1500 µg/litre. Mass spectrometry (detection limit 0.17 µg/litre) can be used to confirm the identity of the compound (*5*).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Air

1,1-Dichloroethane has been detected in urban air at concentrations ranging from 0.4 to 6.1 µg/m^3. A median concentration of 0.22 µg/m^3 was reported for urban, rural, and industrial sites across the United States. Concentrations in the vicinity of industrial sources ranged from 0.23 to 0.56 µg/m^3, and a concentration of 22.5 µg/m^3 was reported near a hazardous waste site. 1,1-Dichloroethane has also been detected in indoor air at a mean concentration of 12.8 µg/m^3 (*3*).

Water

1,1-Dichloroethane was detected in 4.3% of 945 public water supplies in the USA at levels of up to 4.2 µg/litre. It was also detected in private wells used for drinking-water and in surface water and groundwater supplies, generally at levels below 10 µg/litre, although concentrations up to 400 µg/litre have been reported (*3*).

Estimated total exposure and relative contribution of drinking-water

Exposure to 1,1-dichloroethane may occur through drinking-water, but from the point of view of the general population the greatest exposure is usually from the inhalation of ambient air. Based on a median air level of 0.22 µg/m^3, the average inhalation exposure to 1,1-dichloroethane is estimated at 4 µg/day (*3*).

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

The detection of metabolites in the urine following oral exposure and its former use as an anaesthetic provide evidence for the absorption of 1,1-dichloroethane by the oral and inhalation routes (*6*). In general, chlorinated organic solvents are distributed throughout the body following absorption into the blood but preferentially to adipose tissue (*7*). Following intraperitoneal administration of 1,1-dichloroethane to rats, the compound was detected in liver, kidney, lung, and stomach tissues (*8*).

Following oral administration of 1,1-dichloroethane to mice and rats, 29% and 7% was metabolized, respectively (*6*), the major metabolite in both species being carbon dioxide. *In vitro* studies suggest that the primary route of biotransformation involves the hepatic microsomal cytochrome P-450 system, the major metabolite being ethanoic acid (*9,10*). The metabolic capacity of the P-450 system may be exceeded with high oral doses (*3*). Absorbed 1,1-dichloroethane is excreted mainly in the urine and expired air (*6,7*).

EFFECTS ON LABORATORY ANIMALS AND *IN VITRO* TEST SYSTEMS

Acute exposure

Reported oral LD_{50}s in rats range from 0.7 to 14 g/kg of body weight (*11,12*).

Short-term exposure

Groups of five male and five female Osborne-Mendel rats and B6C3F$_1$ mice received 1,1-dichloroethane in corn oil by gavage, 5 days per week for 6 weeks; this was followed by a 2-week observation period (*13*). Dose levels were 0, 562, 1000, 1780, 3160, or 5620 mg/kg of body weight per day for rats and 0, 1000, 1780, 3160, 5620, or 10 000 mg/kg of body weight per day for mice. Body weight was depressed in male rats at 562 and 1000 mg/kg of body weight per day and in female rats at 1780 and 3160 mg/kg of body weight per day. Two female rats in the group receiving 3160 mg/kg of body weight per day and two male and three female mice in that receiving 5620 mg/kg of body weight per day died.

Groups of 10 rats, 10 guinea pigs, four rabbits, and four cats were exposed to 2025 mg/m^3 1,1-dichloroethane by inhalation for 6 h per day, 5 days per week for 13 weeks (*14*). Because no effects were observed in these animals, the exposure concentration was increased to 4050 mg/m^3 for an additional 10B13 weeks. Elevated blood urea nitrogen values were observed in cats only. At termination, histopathological examination revealed renal tubular dilation and degeneration.

Long-term exposure

Groups of Osborne-Mendel rats and B6C3F$_1$ mice were given 1,1-dichloroethane by gavage in corn oil, 5 days per week for 78 weeks, at time-weighted average doses of 382 or 764 mg/kg of body weight per day (male rats), 475 or 950 mg/kg of body weight per day (female rats), 1442 or 2885 mg/kg of body weight per day (male mice), and 1665 or 3331 mg/kg of body weight per day (female mice) (*13*). High mortality was seen in both treated and control animals; mortality in male rats and mice showed a significant dose-related trend. The increased mortality was thought to be related to pneumonia, which was observed in about 80% of the rats.

Male B6C3F$_1$ mice were given 1,1-dichloroethane in drinking-water at concentrations of 835 or 2500 mg/litre (high dose equivalent to about 540 mg/kg of body weight per day) for 52 weeks (*15*). No histopathological changes were observed in the liver, kidneys, or lungs.

Reproductive toxicity, embryotoxicity, and teratogenicity

1,1-Dichloroethane has been found to be embryotoxic but not teratogenic following inhalation exposure. Exposure of pregnant rats to 15.4 or 24.3 g/m^3 1,1-dichloroethane in air 7 h per day on days 6–15 of gestation did not affect the incidence of fetal resorptions or gross or soft tissue anomalies, although a significantly increased incidence of delayed ossification of the sternebrae, reflecting retarded fetal development, was observed in offspring of the rats exposed at 24.3 g/m^3 (*16*).

Mutagenicity and related end-points

1,1-Dichloroethane was found to be mutagenic in several strains of *Salmonella typhimurium* with or without metabolic activation (*17*) but not in others (*3,18*). It was not mutagenic in *Saccharomyces cerevisiae* strains with or without metabolic activation (*3,18*). 1,1-Dichloroethane increased the frequency of DNA viral transformations in Syrian hamster embryo cells (*19*) but did not increase cell transformations in BALB/c-3T3 mouse cells (*20*). 1,1-Dichloroethane was positive in DNA binding assays in mouse and rat organs *in vivo*. Following intraperitoneal injection, it was reported to be covalently bound to macromolecules (DNA, RNA, proteins) in liver, lung, stomach, and kidney tissues of both species (*8*).

Carcinogenicity

Groups of Osborne-Mendel rats and B6C3F$_1$ mice were given 1,1-dichloroethane by gavage in corn oil, 5 days per week for 78 weeks, at time-weighted average doses of 382 or 764 mg/kg of body weight per day (male rats), 475 or 950 mg/kg of body weight per day (female rats), 1442 or 2885 mg/kg of body weight per day (male mice), and 1665 or 3331 mg/kg of body weight per day (female mice) (*13*). Marginally significant dose-related increases in mammary adenocarcinomas and haemangiosarcomas in female rats and a nonsignificant increase in hepatocellular carcinomas in male mice were observed. A statistically significant increase in uterine endometrial stromal polyps (benign tumours) was also observed. Lymphomas of the cervical lymph nodes were reported in 2 of 47 female mice in the high-dose group but not in other groups. The authors concluded that high mortality in all the groups prevented the appearance of late-developing tumours. The results of this study suggest that 1,1-dichloroethane is carcinogenic in rats and mice, but the evidence is not considered conclusive.

1,1-Dichloroethane was administered in drinking-water to male B6C3F$_1$ mice at concentrations of 835 or 2500 mg/litre (the latter is equivalent to about 540 mg/kg of body weight per day) for 52 weeks, either alone or following initiation with diethylnitrosamine (*15*). Lung and liver tumours were found in all groups, but neither the incidence nor the

number of tumours per animal was increased as compared with controls in any treatment group. This was not a lifetime study, and there was a high incidence of spontaneous tumours in controls, so that its value is limited. The authors suggested that 1,1-dichloroethane may be more toxic by gavage than by drinking-water exposure.

EFFECTS ON HUMANS

It can be assumed that inhalation exposures to high concentrations of 1,1-dichloroethane cause central nervous system depression, as the compound was used as an anaesthetic until its use was discontinued because of the occurrence of cardiac arrhythmias at concentrations required for anaesthesia (>100 000 mg/m^3) (*21*).

CONCLUSIONS

The acute toxicity of 1,1-dichloroethane is relatively low, and only limited data on its toxicity are available from short- and long-term studies. There is limited *in vitro* evidence of genotoxicity. One carcinogenicity study by gavage in mice and rats provided no conclusive evidence of carcinogenicity, although there was some evidence for an increased incidence of mammary adenocarcinomas and haemangiosarcomas in treated animals (*13*).
In view of the very limited database on toxicity and carcinogenicity, it is concluded that no guideline value should be proposed.

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