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English only

Trichlorobenzenes in Drinking-water

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

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

Trichlorobenzenes in Drinking-water, Background document for development of WHO *Guidelines for Drinking-water Quality*, is an update of the background document published in the second edition of the GDWQ.

The work of the following working group coordinators was crucial in the development of this document and others in the third edition:

Mr J.K. Fawell, United Kingdom (*Organic and inorganic constituents*)
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The contribution of peer reviewers is greatly appreciated. The draft text was posted on the world wide web for comments from the public. The revised text and the comments were discussed at the Final Task Force Meeting for the third edition of the GDWQ, held on 31 March to 4 April 2003, at which time the present version was finalized. The input of those who provided comments and of participants in the meeting is gratefully reflected in the final text.

The WHO coordinators were as follows:

Dr J. Bartram, Coordinator, Water Sanitation and Health Programme, WHO Headquarters, and formerly WHO European Centre for Environmental Health
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Ms C. Vickers provided a liaison with the International Chemical Safety Programme, WHO Headquarters.

Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

Many individuals from various countries contributed to the development of the GDWQ. The efforts of all who contributed to the preparation of this document and in particular those who provided peer or public domain review comment are greatly appreciated.

Acronyms and abbreviations used in the text

CAS	Chemical Abstracts Service
DNA	deoxyribonucleic acid
LD_{50}	median lethal dose
NOAEL	no-observed-adverse-effect level
TCB	trichlorobenzene
TDI	tolerable daily intake
USA	United States of America

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1. GENERAL DESCRIPTION

1.1 Identity

Compound	*CAS No.*	*Molecular formula*
1,2,3-Trichlorobenzene (1,2,3-TCB)	76-61-6	$C_6H_3Cl_3$
1,2,4-Trichlorobenzene (1,2,4-TCB)	120-82-1	$C_6H_3Cl_3$
1,3,5-Trichlorobenzene (1,3,5-TCB)	108-70-3	$C_6H_3Cl_3$

1.2 Physicochemical properties (1–4)

Property	*1,2,3-TCB*	*1,2,4-TCB*	*1,3,5-TCB*
Melting point (°C)	53–54	17	63–64
Boiling point (°C)	218–219	213.5	208
Water solubility (mg/litre)	12 (22 °C)	19 (22 °C)	5.8 (20 °C)
Log octanol–water partition coefficient	4.04	4.02	4.49
Vapour pressure at 25 °C (kPa)	–	0.04	0.08

1.3 Organoleptic properties

Odour thresholds of 10, 5–30 and 50 µg/litre have been reported for 1,2,3-TCB, 1,2,4-TCB and 1,3,5-TCB, respectively *(5,6)*. A taste and odour threshold concentration of 30 µg/litre has been reported for 1,2,4-TCB *(7)*.

1.4 Major uses

1,2,4-TCB is economically the most important isomer. Industrial-grade TCB, which consists of 93–98% 1,2,4-TCB and the remainder 1,2,3-TCB, is used as an intermediate in chemical synthesis, a solvent, a coolant, a lubricant and a heat-transfer medium; it is also used in polyester dyeing, in termite control preparations and as an insecticide *(8)*.

1.5 Environmental fate

The TCBs are expected to be adsorbed onto soils of high organic content, but not to leach appreciably into groundwater. They are not hydrolysed and are unlikely to biodegrade significantly. Some evaporation may occur from soil surfaces. In water, TCBs are likely to be adsorbed onto sediments and to bioconcentrate in aquatic organisms. Evaporation from water may be a significant removal process *(3)*.

2. ANALYTICAL METHODS

A standard method for chlorobenzenes involves extraction with hexane followed by capillary column gas–liquid chromatography with electron capture detection. Detection limits in tap water and river water are about 0.1 µg/litre for TCBs *(9)*.

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

Levels are likely to be significant only in areas where TCBs are produced. Mean levels of 22–51 ng/m^3 have been reported for three sites in California, USA *(10)*. An average of 181 ng/m^3 was reported in areas where TCBs are produced in the USA *(3)*.

3.2 Water

TCBs have been detected in wastewater, surface water, groundwater and drinking-water *(3)*. In a Canadian river, levels of 2, 7 and 2 µg/litre were reported for 1,2,3-TCB, 1,2,4-TCB and 1,3,5-TCB, respectively *(11)*. Tap water concentrations were reported in the same study, the highest being for 1,2,4-TCB, for which the mean reported level was 2 ng/litre. The maximum value for all isomers found in a groundwater survey in the Netherlands was 1.2 µg/litre *(12)*.

3.3 Food

TCBs tend to accumulate in biological materials rich in lipids, such as fatty tissue and milk; residues at levels of 0.1–4 mg/kg on a fat basis were found in the liver of cod from areas polluted by industrial effluents *(13)*. Mean levels reported in human milk were 1, 1 and 5 µg/kg for 1,3,5-TCB, 1,2,4-TCB and 1,2,3-TCB, respectively *(14)*.

3.4 Estimated total exposure and relative contribution of drinking-water

General population exposure will occur mainly through the inhalation of contaminated air in areas where TCBs are manufactured and from the ingestion of contaminated food, especially fish.

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

All three TCB isomers were readily absorbed following oral administration in rats. High concentrations of the parent compound were found in fat, skin and liver, whereas high levels of metabolites were found in kidney and muscle *(15)*. The major metabolic products are trichlorophenols *(16)*. Species differences appear to exist in the metabolism of TCBs. Rats and rhesus monkeys given 1,2,4-TCB orally and intravenously excreted different urinary metabolites. Excretion was more rapid in rats than in monkeys; after 24 h, rats had excreted 84% of the oral dose in the urine and 11% in the faeces, compared with 40% and <1%, respectively, in monkeys *(17)*. There is also evidence that the TCBs are broad inducers of metabolizing enzymes *(16)*.

5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS

5.1 Acute exposure

TCBs are of low to moderate acute toxicity. Oral LD_{50}s in rodents range from 300 to 800 mg/kg of body weight. Major target organs of acute exposure are the liver and kidneys *(16)*.

5.2 Short-term exposure

In a 13-week study, weanling Sprague-Dawley rats were fed diets containing TCB isomers at 1, 10, 100 or 1000 mg/kg. All three isomers at 1000 mg/kg caused increased relative liver and kidney weights and histological changes in the liver and thyroid of male rats. Males fed 1000 mg of 1,2,3-TCB per kg showed reduced weight gain; no other clinical signs of toxicity were observed. Only 1,2,4-TCB at 1000 mg/kg caused increases in hepatic aminopyrine methyl transferase and aniline hydroxylase activities in males and aminopyrine methyl transferase in females. The serum biochemical and haematological parameters measured were not affected. Only 1,3,5-TCB elicited moderate renal changes in male rats at 1000 mg/kg. Microscopic changes in females were milder than those in males. NOAELs were 100 mg/kg for all three isomers, equal to 7.8 mg/kg of body weight per day (1,2,4-TCB), 7.7 mg/kg of body weight per day (1,2,3-TCB) or 7.6 mg/kg of body weight per day (1,3,5-TCB) *(18)*.

5.3 Long-term exposure

Relevant chronic studies via the oral route have not been carried out. In a 2-year dermal study, S1c:ddy mice administered 0.03 ml of a 30% or 60% solution of 1,2,4-TCB twice a week showed signs of clinical toxicity, decreased survival and keratinization of the epidermis *(19)*. The main causes of death were respiratory infection, amyloidosis and tumours.

5.4 Reproductive and developmental toxicity

No evidence of teratogenic effects was reported when Sprague-Dawley rats were given oral doses of 75, 150 or 300 mg of 1,2,4-TCB per kg of body weight per day or 150, 300 or 600 mg of 1,2,3-TCB or 1,3,5-TCB per kg of body weight per day on days 6–15 of gestation *(20)*. Rats exposed to 0, 25, 100 or 400 mg of 1,2,4-TCB per litre in their drinking-water from the birth of the F_0 generation to the weaning of the F_2 generation did not show any effects on fertility *(21)*.

5.5 Mutagenicity and related end-points

None of the isomers of TCB was mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535 or TA1537, with or without metabolic activation *(22,23)*. All three caused dose-related increases in the formation of micronucleated polychromatic erythrocytes in mice injected with TCBs in corn oil at doses up to 70% of the LD_{50}

(24). It was considered that the effects were due to the clastogenic activity of the TCBs; however, these results have not been confirmed by other workers *(16)*.

5.6 Carcinogenicity

Relevant carcinogenicity studies via the oral route have not been carried out. In the 2-year dermal study in which S1c:ddy mice were given 0.03 ml of a 30% or 60% solution of 1,2,4-TCB twice a week *(19)*, tumours occurred in both experimental and control groups, suggesting that they were spontaneous in origin and not due to the carcinogenic effects of this compound.

6. EFFECTS ON HUMANS

TCBs are moderately toxic when ingested or inhaled. They produce irritation of the skin, eyes and respiratory tract *(8)*. There has been one report of aplastic anaemia in a woman chronically exposed to 1,2,4-TCB from washing work clothes *(25)*.

7. CONCLUSIONS

The TCBs are of moderate acute toxicity. After short-term oral exposure, all three isomers show similar toxic effects, predominantly on the liver. Long-term toxicity and carcinogenicity studies via the oral route have not been carried out, but the data available suggest that all three isomers are non-genotoxic.

A TDI of 7.7 µg/kg of body weight can be calculated by applying an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the short duration of the study) to the NOAEL of 7.7 mg/kg of body weight per day for liver toxicity identified in a 13-week rat study *(18)*. A health-based value of 20 µg/litre (rounded figure) can be calculated for each TCB isomer based on an allocation of 10% of the TDI to drinking-water; because of the similarity in the toxicity of the TCB isomers, the health-based value of 20 µg/litre would apply to total TCBs.

However, because TCBs occur at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value. It should be noted that the health-based value exceeds the lowest reported odour threshold in water.

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