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Carbon Tetrachloride 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

Carbon Tetrachloride 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 Guidelines. The update was prepared by Mr J.K. Fawell and Mr R. Mascarenhas, United Kingdom, to whom special thanks are due.

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 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
cDNA	complementary deoxyribonucleic acid
CYP	cytochrome P-450
DNA	deoxyribonucleic acid
LD_{50}	median lethal dose
NOAEL	no-observed-adverse-effect level
TDI	tolerable daily intake
USA	United States of America

Table of contents

1. GENERAL DESCRIPTION

1.1 Identity

CAS No.:	56-23-5
Molecular formula:	CCl_4

1.2 Physicochemical properties[1] *(IPCS, 1999)*

Property	*Value*
Melting point	-23 °C
Boiling point	76.5 °C
Density	1.594 g/m^3 at 25 °C
Vapour pressure	15.36 kPa at 25 °C
Water solubility	785 mg/litre at 20 °C
Log octanol–water partition coefficient	2.64

1.3 Organoleptic properties

The odour thresholds for carbon tetrachloride in water and air are 0.52 mg/litre and <6.4 mg/m^3, respectively (Amoore & Hautala, 1983).

1.4 Major uses

Carbon tetrachloride is used mainly in the production of chlorofluorocarbon refrigerants, foam-blowing agents and solvents. It is also used in the manufacture of paints, ink, plastics, semi-conductors and petrol additives, as a solvent in metal cleaning and as a grain fumigant, pesticide, fire extinguisher and flame retardant.

The global production of carbon tetrachloride amounted to 960 000 tonnes in 1987. However, since the Montreal Protocol on Substances that Deplete the Ozone Layer (1987) and its amendments (1990 and 1992) established a timetable for the phase-out of the production and consumption of carbon tetrachloride, manufacture has dropped and will continue to drop (UNEP, 1996; IPCS, 1999). All the uses of carbon tetrachloride have tended to be phased out as production has dropped (ATSDR, 1994).

1.5 Environmental fate

Carbon tetrachloride is released mostly into the atmosphere but also into industrial wastewater. In the USA, it has also been disposed of by underground injection into wells (TRI, 1999).

Most carbon tetrachloride released into the environment reaches the atmosphere, where it is uniformly distributed. It does not react with photochemically produced hydroxyl radicals in the troposphere but is principally degraded in the stratosphere,

[1] Conversion factor in air: 1 ppm = 6.4 mg/m^3.

where it is dissociated by short-wavelength ultraviolet radiation to form the trichloromethyl radical and chlorine atoms. It has an estimated half-life of 18–80 years in the atmosphere (Simmonds et al., 1983; IPCS, 1999). The chlorine atoms in carbon tetrachloride interact with oxygen or ozone to produce $ClO^{\cdot}$ groups, and the chlorine atoms and the $ClO^{\cdot}$ groups in turn attack the surrounding ozone (IPCS, 1999).

Carbon tetrachloride dissolved in water does not photodegrade or oxidize in any measurable amount. A large proportion of carbon tetrachloride is lost from surface water by volatilization; it readily migrates from surface water to the atmosphere in a matter of days or weeks. However, levels in anaerobic groundwater may remain elevated for months or even years. Carbon tetrachloride is capable of being adsorbed onto organic matter in soils. Migration to groundwater is possible. Bioaccumulation has not been observed (ATSDR, 1994; IPCS, 1999).

2. ANALYTICAL METHODS

Carbon tetrachloride in drinking-water is determined by purge-and-trap, liquid–liquid extraction or headspace techniques followed by gas chromatography. It is usually detected by electron capture detector or mass spectrometry, the detection limit being about 0.1–0.3 µg/litre (ATSDR, 1994; IPCS, 1999; Kuivinen & Johnsson, 1999).

3. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

3.1 Air

During the period 1980–1990, atmospheric levels of carbon tetrachloride were around 0.5–1.0 µg/m^3 (IPCS, 1999). Outdoor concentrations as high as 3.7 µg/m^3 have been reported near point sources. Indoor concentrations (1 µg/m^3) tend to be higher than outdoor levels (ATSDR, 1994).

3.2 Water

Typical concentrations of carbon tetrachloride in rivers heavily polluted by industrial effluents are in the range of 3.3–14 µg/litre for River Mersey and 0.3–110 µg/litre for the Manchester Ship Canal (Rogers et al., 1992). Even higher values (e.g., 160–1500 µg/litre in the River Rhine and a mean of 75 µg/litre in the River Main, recorded in 1976 in Germany) were the result of direct waste release (BUA, 1990; IPCS, 1999).

Carbon tetrachloride has been identified in a third of US hazardous waste sites proposed for priority listing (ATSDR, 1994). Carbon tetrachloride was detected in leachates from industrial landfills at concentrations ranging from <10 to 92 µg/litre (Brown & Donnelly, 1988).

Groundwater levels range from undetectable to a maximum of 80 µg/litre (WHO, 1999). Much of this variation is because, like the situation with other chlorinated solvents, poor disposal practices in the past have resulted in significant point source

pollution of groundwater. Generally, background levels in drinking-water are less than 1 µg/litre.

In 30 out of 945 drinking-water samples from various cities in the USA, carbon tetrachloride was detected at mean levels ranging from 0.3 to 0.7 µg/litre, with a maximum concentration of 16 µg/litre (Westrick et al., 1984). Drinking-water in Germany was reported to contain an average carbon tetrachloride concentration of <0.1 µg/litre, with a maximum of 1.4 µg/litre (average of 100 towns in 1977) (Bauer, 1981). Lahl et al. (1981) reported an even lower concentration of <0.1 µg/litre in the drinking-water of 50 German cities.

Median concentrations up to 3 µg/litre and a maximum concentration of 39.5 µg/litre were reported in the drinking-water of Galicia, Spain (Freiria-Gándara et al., 1992). Carbon tetrachloride concentrations in tap water in Gdansk, Poland, ranged from not detected to 0.7 µg/litre (Biziuk et al., 1996). In Italy, carbon tetrachloride concentrations in drinking-water averaged 0.2 µg/litre (Aggazzotti & Predieri, 1986). Carbon tetrachloride is an occasional contaminant of the chlorine used for drinking-water disinfection (Palacios et al., 2000).

3.3 Food

According to investigations carried out in Europe and the USA between 1973 and 1989, many foodstuffs contained carbon tetrachloride at concentrations of a few µg/litre or µg/kg (IPCS, 1999). Foods often become contaminated by carbon tetrachloride when they are fumigated with it. However, carbon tetrachloride is now seldom used for this purpose.

3.4 Estimated total exposure and relative contribution of drinking-water

Although available data on concentrations in food are limited, the intake from air is expected to be much greater than that from food or drinking-water. At a typical carbon tetrachloride concentration of 1 µg/m^3 in air, the daily exposure by inhalation is estimated to be about 20 µg for an adult with an air intake of 20 m^3/day. At a typical concentration of 0.5 µg/litre in drinking-water, a daily exposure of 1 µg is estimated for an adult with an average consumption of 2 litres of water per day.

Exposure from contaminated drinking-water can also occur as a result of inhalation of carbon tetrachloride that has volatilized during showering or other domestic water uses, such as clothes washing (McKone, 1987).

4. KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Carbon tetrachloride is well absorbed from the gastrointestinal and respiratory tracts in animals and humans. Dermal absorption of liquid carbon tetrachloride is possible, but dermal absorption of the vapour is slow. Distribution is throughout the whole body, with highest concentrations in liver, brain, kidney, muscle, fat and blood.

Carbon tetrachloride tends to accumulate in fat (Sanzgiri et al., 1997; IPCS, 1999; Benson et al., 2001). Studies comparing uptake after gastric infusion and oral bolus doses in 10% Emulphor show that uptake and tissue levels were less after infusion than after a bolus dose (Sanzgiri et al., 1997).

Several studies have demonstrated that the metabolism of carbon tetrachloride, and hence carbon tetrachloride-induced effects, can be significantly influenced by the dosing vehicle (i.e., corn oil or aqueous emulsion), but there is no agreement as to the extent (Condie et al., 1986; Kim et al., 1990a,b; Narotsky et al., 1994).

The first step in the biotransformation of carbon tetrachloride is catalysed by cytochrome P-450 enzymes (mainly CYP2E1), leading to the formation of the reactive trichloromethyl radical. The radical is oxidized further, forming the even more reactive trichloromethylperoxyl radical, which can react further to form phosgene. Phosgene may be detoxified by reaction with water to produce carbon dioxide or with glutathione or cysteine. Formation of chloroform and dichlorocarbene occurs under anaerobic conditions (McGregor & Lang, 1996; IPCS, 1999).

Covalent binding to macromolecules and lipid peroxidation occur via reactive metabolic intermediates of carbon tetrachloride, in particular the trichloromethylperoxyl radical (IPCS, 1999).

Carbon tetrachloride and its metabolites are excreted primarily in exhaled air and to a lesser extent in the urine and faeces (IPCS, 1999).

Studies on the uptake, tissue distribution and elimination of carbon tetrachloride by mice, rats and hamsters have shown that rats are the least sensitive to the hepatotoxic effects of repeated inhaled carbon tetrachloride (32–770 mg/m^3) and are notably less sensitive than mice to the hepatocarcinogenic effects (Benson et al., 2001) and that this species sensitivity correlates with carbon tetrachloride equivalent dose to liver and with the ability to metabolize carbon tetrachloride (Thrall et al., 2000; Benson et al., 2001). Predictions obtained from physiologically based pharmacokinetic models suggest that metabolism of carbon tetrachloride in the average rat is greater than that in the average human (Delic et al., 2000). In contrast, Zangar et al. (2000) showed that *in vitro* hepatic microsomal metabolic parameters for human liver microsomes (carbon tetrachloride metabolic rate constants, K_m and V_{max}) varied less than 2-fold from those for rats, mice and hamsters.

5. EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS

The primary targets for carbon tetrachloride toxicity are liver and kidney. The severity of the effects on the liver depends on a number of factors, such as species susceptibility, route and mode of exposure, diet and co-exposure to other compounds, in particular ethanol. Furthermore, it appears that pretreatment with various compounds, such as phenobarbital and vitamin A, enhances hepatotoxicity, while other compounds, such as vitamin E, reduce the hepatotoxic action of carbon tetrachloride (IPCS, 1999).

5.1 Acute exposure

Oral LD_{50} values (14 days of observation) for rats were reported as 2821 mg/kg of body weight (unknown vehicle; Smyth et al., 1970) and 10 054 mg/kg of body weight (in corn oil; Kennedy et al., 1986).

5.2 Short-term exposure

Hepatotoxic effects (increased serum enzymes and histopathology) were observed in rats given carbon tetrachloride in corn oil by gavage at daily doses of 20 mg/kg of body weight and higher for 9 days. The same effects were observed in rats given oral doses of 10 mg/kg of body weight per day, 5 days per week, for 12 weeks. No measurable adverse effects were observed in rats given 1 mg/kg of body weight per day for 12 weeks (Bruckner et al., 1986).

Hepatotoxicity (increased serum enzymes, increased organ weight and pathological changes) was observed in male and female CD-1 mice given carbon tetrachloride in corn oil by gavage at doses of 625, 1250 or 2500 mg/kg of body weight per day for 14 consecutive days. After 90 days, hepatotoxic effects were observed in animals that had ingested 12, 120, 540 or 1200 mg/kg of body weight per day (Hayes et al., 1986).

Male and female CD-1 mice were given carbon tetrachloride at 0, 1.2, 12 or 120 mg/kg of body weight per day for 90 days (5 days per week) by gavage in corn oil or as an aqueous suspension in 1% polysorbate 60 (Condie et al., 1986). A significant increase in serum enzyme activity was detected at 12 and 120 mg/kg of body weight per day in the corn oil groups compared with the polysorbate 60 groups. Liver weights and liver to body weight ratios were significantly greater at 120 mg/kg of body weight per day. Hepatocellular changes (e.g., necrosis, fat) occurred at 12 and 120 mg/kg of body weight per day and were more frequently observed in the corn oil groups. Use of a corn oil vehicle yielded a NOAEL that was an order of magnitude lower than that obtained when the polysorbate 60 suspension was used (12 versus 1.2 mg/kg of body weight per day).

5.3 Long-term exposure

Carbon tetrachloride at doses of 0, 80 or 200 mg/kg of diet (high dose equivalent to about 10–18 mg/kg of body weight per day) was fed to rats (18 per sex, strain not given) until sacrifice at 2 years (Alumot et al., 1976). Although no adverse effects were observed, tissues were not examined microscopically, liver weights were not measured and survival was below 50% at 21 months.

5.4 Reproductive and developmental toxicity

There are no adequate reproductive toxicity studies on carbon tetrachloride. No effects on the reproductive system were noted in rats fed diets containing carbon tetrachloride at 80 or 200 mg/kg (equivalent to 10–18 mg/kg of body weight) (Alumot

et al., 1976), but tissues were not examined microscopically. Degeneration of testicular germinal epithelium has been reported in rats exposed to air concentrations of 1280 mg/m^3 or above (Adams et al., 1952). An intraperitoneal dose of 2400 mg/kg of body weight resulted in adverse effects on testicular function in rats (Chatterjee, 1966). In a study with similar design with female rats, effects on the reproductive system were seen 10 days after dosing.

Available data, although limited, suggest that the fetus is not preferentially sensitive to carbon tetrachloride and that effects of carbon tetrachloride on fetal development and postnatal survival are likely to be secondary to maternal toxicity (IPCS, 1999). When carbon tetrachloride was administered to F-344 rats by gavage on gestation days 6–15 at 0, 25, 50 or 75 mg/kg of body weight per day in corn oil or aqueous vehicle, the former was more toxic to the dams. Full litter resorption was observed at both 50 and 75 mg/kg of body weight per day with both vehicles but was significantly greater, at the highest dose, when carbon tetrachloride was administered in corn oil than when administered in an aqueous vehicle (Narotsky et al., 1997a,b).

Oral administration of 82.6 or 826.3 mg of carbon tetrachloride per kg of body weight per day in corn oil to B6D2F$_1$ mice for 5 consecutive days beginning on day 1, 6 or 11 of gestation resulted in no detectable effects on maternal or neonatal parameters and no apparent adverse effects on development (Hamlin et al., 1993).

5.5 Mutagenicity and related end-points

The genotoxicity of carbon tetrachloride has been extensively reviewed (IPCS, 1999).

Carbon tetrachloride was not mutagenic to *Salmonella typhimurium* in a large number of studies. It did, however, induce DNA damage and mutations in single studies with *Escherichia coli*. In fungi, it induced intrachromosomal and mitotic recombination. However, it did not induce aneuploidy in one study on the yeast *Saccharomyces cerevisiae*, although aneuploidy was induced in another single study with *Aspergillus nidulans*. In the only study with *Drosophila melanogaster*, sex-linked recessive lethal mutations were not induced by carbon tetrachloride (IPCS, 1999).

There is little evidence for the induction *in vitro* of DNA damage, unscheduled DNA synthesis, sister chromatid exchange or chromosomal aberrations (IPCS, 1999).

In mammalian *in vivo* tests, carbon tetrachloride did induce DNA strand breakage in one study (in rat hepatocytes) but not in four others and did not induce a) unscheduled DNA synthesis in rat hepatocytes; b) micronuclei in mouse hepatocytes, bone marrow cells or peripheral blood erythrocytes; c) chromosomal aberrations in mouse bone marrow; or d) aneuploidy in mouse hepatocytes. Binding of carbon tetrachloride to liver cell DNA has been observed in rats, mice and Syrian hamsters treated *in vivo* (IPCS, 1999).

Effects in mammalian cells indicate damage during cytokinesis. This type of damage could result from interactions of, for example, the trichloromethyl radical with

proteins, rather than DNA, and could be induced secondarily to the toxicity of carbon tetrachloride (McGregor & Lang, 1996). No carbon tetrachloride–DNA adduct identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995). Consequently, strand breakage and aneuploidy could arise from the effects of lipid peroxidation products rather than carbon tetrachloride or its metabolites (IPCS, 1999).

In mammalian *in vitro* assays, carbon tetrachloride induced cell transformation in a single study with Syrian hamster cells and centromere-positive-staining micronuclei in human cell lines expressing cDNAs for CYP1A2, CYP2A6, CYP3A4, epoxide hydrolase or CYP2E1. The AHH-1 cell line constitutively expressing CYP1A1 showed no increase in either total micronucleus frequency or centromere-staining micronucleus frequency (Doherty et al., 1996).

On the basis of available data, carbon tetrachloride can be considered to be a non-genotoxic compound (IPCS, 1999).

5.6 Carcinogenicity

In experiments with mice and rats, carbon tetrachloride proved to be capable of inducing hepatomas and hepatocellular carcinomas. The doses inducing hepatic tumours were higher than those inducing cell toxicity. It is likely that the carcinogenicity of carbon tetrachloride is secondary to its hepatotoxic effects (IPCS, 1999).

In a number of studies, the development of liver tumours (primarily hepatomas and hepatocellular carcinomas) in several animal species, including hamsters, mice and rats, has been reported following oral, subcutaneous and inhalation exposure. In general, the first tumours appeared only at doses greater than those causing cell toxicity (IPCS, 1999).

After inbred strain L mice were exposed to oral doses of 0.04 ml (approximately 64 mg) of carbon tetrachloride 2–3 times per week for 4 months, hepatomas developed in 47% of the treated animals, compared with 1% of controls (Edwards, 1941).

Groups of $B6C3F_1$ mice (50 per sex) were given carbon tetrachloride at 0, 1250 or 2500 mg/kg of body weight per day, 5 times per week for 78 weeks, via corn oil gavage, and Osborne-Mendel rats were given 47 or 94 mg/kg of body weight per day (males) and 80 or 159 mg/kg of body weight per day (females) via the same dosing regimen (Weisburger, 1977). The incidence of hepatocellular carcinomas was markedly increased in treated mice (96–100%) but only slightly in rats (2–8%) compared with controls (0–6%).

In a study in which Syrian golden hamsters (10 per sex per group) were exposed to oral doses of carbon tetrachloride at 6.25–12.5 µl/day (approximately 10–20 mg/day) for 43 weeks, all animals that survived the treatment period (5 per sex) developed liver cell carcinomas (Della Porta et al., 1961).

6. EFFECTS ON HUMANS

Single oral doses of 2.5–15 ml (57–343 mg/kg of body weight) do not usually produce severe effects. Some adults suffer adverse effects (including fat accumulation in the liver and renal swelling) from the ingestion of as little as 1.5 ml (34 mg/kg of body weight). A dose of 0.18–0.92 ml (29–150 mg/kg of body weight) may be fatal in children. Alcohol consumption potentiates carbon tetrachloride-induced hepatic and renal effects in humans (ATSDR, 1994; IPCS, 1999).

Occupational exposure to carbon tetrachloride at concentrations of 128–512 mg/m^3 for 2–3 months produced neurological effects (nausea, depression, dyspepsia and narcosis) in workers. Hepatic and renal effects similar to those described for acute oral exposures have been reported after short-term exposures to 1280 mg/m^3 (ATSDR, 1994).

A number of epidemiological studies have examined potential cause–effect relationships between carbon tetrachloride exposure and the incidence of cancer (IARC, 1999). Because these studies are all characterized by mixed exposures and a lack of specific carbon tetrachloride exposure data, any contribution from carbon tetrachloride cannot be reliably identified (IPCS, 1999).

In three occupationally based studies that collected information on non-Hodgkin lymphoma, associations with exposure to carbon tetrachloride were suggested, but the associations were not strong statistically (Blair et al., 1990, 1998; IARC, 1999). A nested case–control study (Bond et al., 1986) of lung cancer in a cohort of chemical workers showed no association with exposure to carbon tetrachloride. Four population-based case–control studies examined associations of carbon tetrachloride with chronic lymphocytic leukaemia (Linet et al., 1987), brain cancer (Heinemann et al., 1994), female breast cancer (Cantor et al., 1995) and intraocular melanoma (Holly et al., 1996), but the findings were generally unremarkable (IARC, 1999).

7. GUIDELINE VALUE

Carbon tetrachloride is classified by IARC (1999) as being possibly carcinogenic to humans (Group 2B). There is sufficient evidence that carbon tetrachloride is carcinogenic in laboratory animals, but inadequate evidence in humans.

Many genotoxicity assays have been conducted with carbon tetrachloride. On the basis of available data, carbon tetrachloride can be considered to be a non-genotoxic compound. Carbon tetrachloride induces hepatomas and hepatocellular carcinomas in mice and rats. The doses inducing hepatic tumours are higher than those inducing cell toxicity. The available data indicate that the hepatic tumours are induced by a non-genotoxic mechanism (IPCS, 1999), and it was considered acceptable to use a TDI approach to derive a guideline value for carbon tetrachloride.

On the basis of the study by Bruckner et al. (1986), in which a NOAEL of 1 mg/kg of body weight per day was observed in a 12-week oral study on rats, and incorporating a conversion factor of 5/7 for daily dosing and applying an uncertainty factor of 500 (100 for inter- and intraspecies variation, 10 for the duration of the study and a modifying factor of 0.5 because it was a bolus study), a TDI of 1.4 µg/kg of body weight is obtained (IPCS, 1999).

The guideline value, based on 10% allocation of the TDI to drinking-water and assuming a 60-kg adult drinking 2 litres of water per day, is 4 µg/litre (rounded figure). This value is lower than the range of values associated with lifetime upper-bound excess cancer risks of 10^{-4}, 10^{-5} and 10^{-6} calculated by linear extrapolation.

Carbon tetrachloride can be removed from water by air stripping (Wood et al., 1990); greater than 95% removal and a treated water concentration of 1 µg/litre or less should be achievable by this technique. Carbon tetrachloride can also be removed by adsorption onto activated carbon (Bhowmick & Semmens, 1994).

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