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Preface

Between 1993 and 1997, the World Health Organization (WHO) published the second edition of *Guidelines for drinking-water quality* in three volumes: Volume 1, *Recommendations*, in 1993, Volume 2, *Health criteria and other supporting information*, in 1996, and Volume 3, *Surveillance and control of community supplies*, in 1997. Development of the *Guidelines* in this second edition was organized and carried out jointly by WHO headquarters and the WHO Regional Office for Europe.

At the Final Task Group Meeting (Geneva, Switzerland, 21-25 September 1992), when the second edition of the *Guidelines* was approved, it was agreed to establish a continuing process of updating, with a number of chemical substances and microbiological agents subject to periodic evaluation. Addenda containing these evaluations will be issued as necessary until the third edition of the *Guidelines* is published, approximately 10 years after the second edition.

In 1995, a Coordinating Committee for the Updating of WHO *Guidelines for drinking-water quality* agreed on the framework for the updating process and established three working groups to support the development of addenda and monographs on chemical aspects, microbiological aspects, and protection and control of water quality. The Committee selected the chemical substances to be evaluated in the first addendum, designated coordinators for each major group of chemicals, and identified lead institutions for the preparation of health criteria documents evaluating the risks for human health from exposure to the particular chemicals in drinking-water. Institutions from Canada, Finland, France, Germany, the Netherlands, Sweden, the United Kingdom, and the USA, as well as the ILO/UNEP/WHO International Programme on Chemical Safety (IPCS), prepared the requested health criteria documents.

Under the responsibility of the designated coordinators for each chemical group, 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 1997 Working Group Meeting on Chemical Substances in Drinking-Water. The Working Group reviewed the health risk assessments and, where appropriate, decided upon guideline values.

During the preparation of draft health criteria documents and at the 1997 Working Group Meeting, careful consideration was invariably given to previous risk assessments carried out by IPCS in its Environmental Health Criteria monographs, 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 nitrate and nitrite in addition to food additives).

Evaluations of chemical substances given in this addendum supersede evaluations of the same substances previously published in Volume 1 of the *Guidelines*. An addendum¹ to Volume 2 of the *Guidelines* contains the criteria monographs prepared for each substance or contaminant covered in this publication; the guideline values are based on these.

¹ Unpublished document WHO/EOS/98.1, available from Division of Operational Support in Environmental Health, World Health Organization, 1211 Geneva 27, Switzerland.

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The work of the following coordinators was crucial in the development of this first addendum on chemical substances in drinking-water:

P. Chambon, Health Environment Hygiene Laboratory of Lyon, Lyon, France (inorganic constituents)

U. Lund, Water Quality Institute, Horsholm, Denmark (organic constituents)

H. Galal-Gorchev, Urban Environmental Health, World Health Organization, Geneva, Switzerland (pesticides)

E. Ohanian, Environmental Protection Agency, Washington, DC, USA (disinfectants and disinfectant by-products)

The coordinators for the overall administrative and technical aspects of this addendum were, respectively, J. Kenny and H. Galal-Gorchev, Urban Environmental Health, WHO, Geneva, Switzerland.

Ms Maria Sheffer of Ottawa, Canada, was responsible for the scientific editing of the addendum.

Special thanks are due to the authors and their institutions for the preparation of draft health criteria documents. The following institutions prepared such health criteria documents: Health Canada; National Public Health Institute, Finland; Health Environment Hygiene Laboratory of Lyon, France; Fraunhofer Institute for Toxicology and Aerosol Research, Germany; National Institute of Public Health and the Environment, Netherlands; National Food Administration, Sweden; International Programme on Chemical Safety, Switzerland; Water Research Centre, England; and the Environmental Protection Agency, USA.

The preparation of this addendum was made possible by the financial support afforded to WHO by Canada, Japan, and the USA.

A financial contribution from the European Commission for the convening of the Working Group Meeting on Chemical Substances in Drinking-Water is gratefully acknowledged.

The preparation of the first addendum to the *Guidelines for drinking-water quality* involved the participation of numerous institutions and experts, whose names appear in Annex 1. Their work was central to the completion of this addendum and is much appreciated.

Acronyms and abbreviations used in the text¹

¹ These acronyms and abbreviations are used without definition in the text.

ADI	acceptable daily intake
DNA	Deoxyribonucleic acid
FAO	Food and Agriculture Organization of the United Nations
IARC	International Agency for Research on Cancer
ILO	International Labour Organisation
IPCS	ILO/UNEP/WHO International Programme on Chemical Safety
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMP	Joint Meeting on Pesticides
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LOAEL	lowest-observed-adverse-effect level
NOAEL	no-observed-adverse-effect level
TDI	tolerable daily intake
UNEP	United Nations Environment Programme
WHO	World Health Organization

Introduction

Chemical substances evaluated in this addendum were selected by the 1995 Coordinating Committee for the Updating of WHO *Guidelines for drinking-water quality* for one or more of the following reasons:

- Adequate data were not available to allow a guideline value to be derived, or only a provisional guideline value could be derived, in the second edition of the *Guidelines*.
- The substance was recommended for evaluation by the Task Group convened to finalize the second edition of the *Guidelines*.
- New health risk assessments were available from IPCS through its Environmental Health Criteria monographs, from JMPR, or from JECFA.
- A new evaluation of the carcinogenic risk of the chemical was available from IARC.
- Requests to evaluate the chemical were made to the WHO Secretariat.

Concepts of guideline value and provisional guideline value, assumptions made, and scientific principles for the assessment of risk to human health from exposure to chemicals in drinking-water used in this addendum are described in Volume 1, *Recommendations*, of the second edition of the *Guidelines*. Only a brief summary of the approaches used to derive the guideline values is given here.

In developing the guideline values for potentially hazardous chemicals, a daily consumption of 2 litres of drinking-water by a person weighing 60 kg was generally assumed. Where it was judged that infants and children were at a particularly high risk from exposure to certain chemicals, the guideline values were derived on the basis of a 5-kg infant consuming 0.75 litre per day or a 10-kg child consuming 1 litre per day.

For compounds showing a threshold for toxic effects, a TDI approach was used to derive the guideline value. A portion of the TDI was allocated to drinking-water, based on potential exposure from other sources, such as food and air. Where information on other sources of exposure was not available, an arbitrary (default) value of 10% of the TDI was allocated to drinking-water.

For compounds considered to be genotoxic carcinogens, guideline values were determined using a mathematical model. The guideline values presented in this addendum to Volume 1 are the concentrations in drinking-water associated with an estimated excess lifetime cancer risk of 10^{-5} (one additional cancer case per 100 000 of the population ingesting drinking-water containing the substance at the guideline value for 70 years). In the addendum to Volume 2, concentrations associated with excess lifetime cancer risks of 10^{-4} , 10^{-5} , and 10^{-6} are presented to emphasize the fact that each country should select its own appropriate risk levels.

It is emphasized that the guideline values recommended are not mandatory limits. Such limits should be set by national or regional authorities, using a risk - benefit approach and taking into consideration local environmental, social, economic, and cultural conditions.

Inorganic constituents

Aluminium

Aluminium is the most abundant metallic element and constitutes about 8% of the earth's crust. Aluminium salts are widely used in water treatment as coagulants to reduce organic matter, colour, turbidity, and microorganism levels. Such use may lead to increased concentrations of aluminium in finished water. Where residual concentrations are high, undesirable colour and turbidity may ensue. Concentrations of aluminium at which such problems may occur are highly dependent on a number of water-quality parameters and operational factors at the water treatment plant. Aluminium intake from foods, particularly those containing aluminium compounds used as food additives, represents the major route of aluminium exposure for the general public. The contribution of drinking-water to the total oral exposure to aluminium is usually less than 5% of the total intake.

In humans, aluminium and its compounds appear to be poorly absorbed, although the rate and extent of absorption have not been adequately studied. The degree of aluminium absorption depends on a number of parameters, such as the aluminium salt administered, pH (for aluminium speciation and solubility), bioavailability, and dietary factors. These parameters should be taken into consideration during tissue dosimetry and response assessment. The use of currently available animal studies to develop a guideline value for aluminium is not appropriate because of these specific toxicokinetic/dynamic considerations.

There is little indication that orally ingested aluminium is acutely toxic to humans despite the widespread occurrence of the element in foods, drinking-water, and many antacid preparations. It has been hypothesized that aluminium exposure is a risk factor for the development or acceleration of onset of Alzheimer disease (AD) in humans. The Environmental Health Criteria document for aluminium (WHO, 1997) concludes that:

"On the whole, the positive relationship between aluminium in drinking-water and AD, which was demonstrated in several epidemiological studies, cannot be totally dismissed. However, strong reservations about inferring a causal relationship are warranted in view of the failure of these studies to account for demonstrated confounding factors and for total aluminium intake from all sources.

Taken together, the relative risks for AD from exposure to aluminium in drinking-water above 100 µg/litre, as determined in these studies, are low (less than 2.0). But, because the risk estimates are imprecise for a variety of methodological reasons, a population-attributable risk cannot be calculated with precision. Such imprecise predictions may, however, be useful in making decisions about the need to control exposures to aluminium in the general population."

Owing to the limitations of the animal data as a model for humans and the uncertainty surrounding the human data, a health-based guideline value for aluminium cannot be derived at this time.

The beneficial effects of the use of aluminium as a coagulant in water treatment are recognized. Taking this into account, and considering the health concerns about aluminium (i.e. its potential neurotoxicity), a practicable level is derived, based on optimization of the coagulation process in drinking-water plants using aluminium-based coagulants, to minimize aluminium levels in finished water.

Several approaches are available for minimizing residual aluminium concentrations in treated water. These include use of optimum pH in the coagulation process, avoiding excessive

aluminium dosage, good mixing at the point of application of the coagulant, optimum paddle speeds for flocculation, and efficient filtration of the aluminium floc. Under good operating conditions, concentrations of aluminium of 0.1 mg/litre or less are achievable in large water treatment facilities. Small facilities (e.g. those serving fewer than 10 000 people) might experience some difficulties in attaining this level, because the small size of the plant provides little buffering for fluctuation in operation; moreover, such facilities often have limited resources and limited access to the expertise needed to solve specific operational problems. For these small facilities, 0.2 mg/litre or less is a practicable level for aluminium in finished water.

Boron

Boron compounds are used in the manufacture of glass, soaps, and detergents, and as flame retardants. Concentrations of boron in water vary widely and depend on the surrounding geology and wastewater discharges.

Boric acid and borax are absorbed from the gastrointestinal tract and the respiratory tract, as indicated by increased levels of boron in the blood, tissues, or urine or by systemic toxic effects of exposed individuals or laboratory animals. Clearance of boron compounds is similar in humans and animals. Elimination of borates from the blood is largely by excretion; 90% or more of the administered dose is eliminated via the urine, regardless of the route of administration. Excretion is relatively rapid, occurring over a period of a few, or possibly several, days.

Short- and long-term oral exposures to boric acid or borax in laboratory animals have demonstrated that the male reproductive tract is a consistent target of toxicity. Testicular lesions have been observed in rats, mice, and dogs given boric acid or borax in food or drinking-water. Developmental toxicity has been demonstrated experimentally in rats, mice, and rabbits. In a developmental toxicity study in rats, the NOAEL was 9.6 mg of boron per kg of body weight per day, based on a decrease in fetal body weight at the next higher dose (13 mg of boron per kg of body weight per day).

Negative results in a large number of mutagenicity assays indicate that boric acid and borax are not genotoxic. In long-term studies in mice and rats, boric acid and borax caused no increase in tumour incidence.

The TDI of boron is derived by dividing the NOAEL (9.6 mg of boron per kg of body weight per day) for the critical effect, which is developmental toxicity (decreased fetal body weight in rats), by an appropriate uncertainty factor, which is judged to be $10 \times 6 = 60$. The value of 10 for interspecies variation (animals to humans) was adopted because of lack of toxicokinetic and toxicodynamic data to allow deviation from this default value. The intraspecies (individual variations) factor of 10 (default value) is made up of two components, 3.2 each, for the inter-individual variability in toxicodynamics and toxicokinetics for a particular compound in humans. However, available toxicokinetic data support reduction of the default value for intraspecies variation from 3.2 to 1.8; there are no data to serve as a basis for replacement of the default value of 3.2 for the toxicodynamic component of the uncertainty factor for intraspecies variation. Hence, the total uncertainty factor for intraspecies variation is $1.8 \times 3.2 = 5.7$ (rounded to 6).

Using an uncertainty factor of 60, the TDI is therefore 0.16 mg of boron per kg of body weight¹. With an allocation of 10% of the TDI to drinking-water and assuming a 60-kg adult consuming 2 litres of drinking-water per day, the guideline value is 0.5 mg/litre (rounded figure).

¹ The Working Group on Chemical Substances in Drinking-Water took note of the lower uncertainty factor proposed by an IPCS Task Group (see: *Boron*. Geneva, World Health Organization, 1998: 146-148 (Environmental Health Criteria, No. 204)), but decided to use the more conservative factor of 60 for the purposes of recommending a guideline value for boron in drinking-water.

Conventional water treatment (coagulation, sedimentation, filtration) does not significantly remove boron, and special methods would have to be installed in order to remove boron from waters with high concentrations. It may be possible to achieve substantial reduction with ion exchange and reverse osmosis processes, but these are likely to be prohibitively expensive. Blending with low-boron water supplies might be the only economical method to reduce high boron concentrations.

The guideline value of 0.5 mg/litre is designated as provisional because, with the treatment technology available, it will be difficult to achieve in areas with high natural boron levels.

Copper

Copper and its compounds are used in electrical wiring, water pipes, cooking utensils, and electroplating, and as algicides and food additives. Copper concentrations in drinking-water vary widely as a result of variations in pH, hardness, and copper availability in the distribution system. Levels of copper in running water tend to be low, whereas those of standing or partially flushed water samples are more variable and can be substantially higher, particularly in areas where the water is soft and corrosive. Adult intake of copper from food is usually 1-2 mg/day and may be considerably increased by consumption of standing or partially flushed water from a system that contains copper pipes or fittings.

Copper is an essential nutrient, required for the proper functioning of many important enzyme systems. In mammals, absorption of copper occurs in the upper gastrointestinal tract and is controlled by a complex homeostatic process. Absorption is influenced by the presence of competing metals, dietary proteins, fructose, and ascorbic acid. The major excretory pathway for absorbed copper is bile. In humans, the highest concentrations of copper are found in the liver, brain, heart, kidney, and adrenal glands. The liver of newborn infants contains about 10 times as much copper as the adult liver and accounts for 50-60% of the total body copper.

Copper utilization is affected by a number of genetic disorders. The genetic abnormalities associated with Menke syndrome, Wilson disease, and aceruloplasminaemia are fairly well understood, and there is some evidence to suggest a genetic basis for Indian childhood cirrhosis and idiopathic copper toxicosis.

Acute gastrointestinal effects may result from exposure to copper in drinking-water, although the levels at which such effects occur are not defined with any precision. Long-term intake of copper in the diet in the range 1.5-3 mg/day has no apparent adverse effects. Daily intake of copper below this range can lead to anaemia, neutropenia, and bone demineralization in malnourished children. Adults are more resistant than children to the symptoms of copper deficiency.

The IPCS Task Group responsible for preparation of the Environmental Health Criteria monograph for copper concluded that:

"The upper limit of the AROI [acceptable range of oral intake] in adults is uncertain but it is most likely in the range of several but not many mg per day... (several meaning more than 2 or 3 mg/day). This evaluation is based solely on studies of gastrointestinal effects of copper-contaminated drinking-water. A more specific value for the upper AROI could not be confirmed for any segment of the general population... The available data on toxicity in animals were considered unhelpful in establishing the upper limit of the AROI, due to uncertainty about an appropriate model for humans."

A copper level of 2 mg/litre in drinking-water should not cause any adverse effects and provides an adequate margin of safety. The epidemiological and clinical studies conducted to date are too limited to allow a clear effect level to be established with any accuracy. Thus, it is recommended that this guideline value for copper of 2 mg/litre remain provisional as a result of uncertainties in

the dose - response relationship between copper in drinking-water and acute gastrointestinal effects in humans. It is also noteworthy that copper is an essential element.

It is stressed that the outcome of epidemiological studies in process in Chile, Sweden, and the USA may permit more accurate quantification of effect levels for copper-induced toxicity in humans, including sensitive subpopulations.

Staining of laundry and sanitary ware occurs at copper concentrations above 1 mg/litre. At levels above 5 mg/litre, copper also imparts a colour and an undesirable bitter taste to water.

Nickel

Nickel is used mainly in the production of stainless steel and nickel alloys. Food is the dominant source of nickel exposure in the non-smoking, non-occupationally exposed population; water is generally a minor contributor to the total daily oral intake. However, where there is heavy pollution or use of certain types of kettles, of non-resistant material in wells, or of water that has stood for an extended time in water pipes, the nickel contribution from water may be significant.

As regards health risks, inhalation is an important route of exposure to nickel and its salts; IARC concluded that inhaled nickel compounds are carcinogenic to humans (Group 1) and metallic nickel is possibly carcinogenic (Group 2B). However, there is a lack of evidence of a carcinogenic risk from oral exposure to nickel.

In several limited studies in rats, the NOAEL was approximately 5 mg of nickel per kg of body weight per day. In a recent careful two-generation study in rats, dose-related increases in perinatal mortality were observed, giving a LOAEL of 1.3 mg/kg of body weight per day in the second litter, whereas the LOAEL in the first litter was 31.6 mg/kg of body weight per day. These variations in response between successive litters make it difficult to draw firm conclusions from this study. In addition, a NOAEL of 7 mg of nickel per kg of body weight per day was derived from a more limited two-generation study in rats.

The guideline value for nickel of 0.02 mg/litre is maintained because, on the basis of the available data, it is considered to provide sufficient protection for individuals who are sensitive to nickel. Owing to uncertainties about the effect level for perinatal mortality, however, the value is considered to be provisional.

Nitrate and nitrite

Nitrate and nitrite are naturally occurring ions that are part of the nitrogen cycle. Nitrate is used mainly in inorganic fertilizers, and sodium nitrite is used as a food preservative, especially in cured meats. The nitrate concentration in groundwater and surface water is normally low but can reach high levels as a result of agricultural runoff, refuse dump runoff, or contamination with human or animal wastes. Chloramination may give rise to the formation of nitrite within the distribution system, and the concentration of nitrite may increase as the water moves towards the extremities of the system. Nitrification in distribution systems can increase nitrite levels, usually by 0.2-1.5 mg/litre, but potentially by more than 3 mg/litre.

The toxicity of nitrate to humans is mainly attributable to its reduction to nitrite. The major biological effect of nitrite in humans is its involvement in the oxidation of normal haemoglobin (Hb) to methaemoglobin (metHb), which is unable to transport oxygen to the tissues. The reduced oxygen transport becomes clinically manifest when metHb concentrations reach 10% or more of normal Hb concentrations; the condition, called methaemoglobinaemia, causes cyanosis and, at higher concentrations, asphyxia. The normal metHb level in humans is less than 2%; in infants under 3 months of age, it is less than 3%.

The Hb of young infants is more susceptible to methHb formation than that of older children and adults; this is believed to be the result of the large proportion of fetal Hb, which is more easily oxidized to methHb, still present in the blood of infants. In addition, there is a deficiency in infants of the methHb reductase responsible for the reduction of methHb to Hb. The net result is that a given dose of nitrite causes higher methHb formation in infants than in adults. When bottle-fed, these young infants are also more at risk because of a relatively high intake of nitrate and, under certain conditions, a higher reduction of nitrate to nitrite by gastric bacteria because of low gastric acidity. The higher reduction of nitrate to nitrite in young infants is not very well quantified; it appears that gastrointestinal infections increase the risk of higher yield of nitrite and thus a higher methHb formation.

There is no evidence for an association between nitrite and nitrate exposure in humans and the risk of cancer.

In 1995 JECFA re-evaluated the chronic health effects of nitrate and nitrite, confirming the previous ADI of 0-3.7 mg/kg of body weight for nitrate ion and establishing an ADI of 0-0.06 mg/kg of body weight for nitrite ion. However, it was noted that these ADI values do not apply to infants below the age of 3 months.

For methaemoglobinaemia in infants (an acute effect), the existing guideline value for nitrate ion of 50 mg/litre was confirmed. For nitrite, human data reviewed by JECFA support the current provisional guideline value of 3 mg/litre, based on induction of methaemoglobinaemia in infants. Toxic doses of nitrite responsible for methaemoglobinaemia ranged from 0.4 to more than 200 mg/kg of body weight. Following a conservative approach by applying the lowest level of the range (0.4 mg/kg of body weight), a body weight of 5 kg for an infant, and a drinking-water consumption of 0.75 litre, a guideline value for nitrite ion of 3 mg/litre (rounded figure) can be derived. Because of the possibility of the simultaneous occurrence of nitrite and nitrate in drinking-water, the sum of the ratios of the concentrations (C) of each to its guideline value (GV) should not exceed 1:

$$\frac{C_{\text{nitrite}}}{GV_{\text{nitrite}}} + \frac{C_{\text{nitrate}}}{GV_{\text{nitrate}}} \leq 1$$

It seems prudent to propose a guideline value for nitrite associated with chronic exposure based on JECFA's analysis of animal data showing nitrite-induced morphological changes in the adrenals, heart, and lungs. Using JECFA's ADI of 0.06 mg/kg of body weight per day, assuming a 60-kg adult ingesting 2 litres of drinking-water per day, and allocating 10% of the ADI to drinking-water, a guideline value of 0.2 mg of nitrite ion per litre (rounded figure) can be calculated. However, owing to the uncertainty surrounding the relevance of the observed adverse health effects for humans and the susceptibility of humans compared with animals, this guideline value should be considered provisional.

Because of known interspecies variation in the conversion of nitrate to nitrite, the animal model was not considered appropriate for use in human risk assessment for nitrate.

All water systems that practise chloramination should closely and regularly monitor their systems to verify disinfectant levels, microbiological quality, and nitrite levels. If nitrification is detected (e.g. reduced disinfectant residuals and increased nitrite levels), steps should be taken to modify the treatment train or water chemistry in order to maintain a safe water quality. Efficient disinfection must never be compromised.

Uranium¹

¹ This review addresses only the chemical aspects of uranium toxicity. Information pertinent to the derivation of a guideline based on radiological effects is presented in the second edition of the *Guidelines for drinking-water quality*.

Uranium is used mainly as fuel in nuclear power stations. It is present in the environment as a result of leaching from natural deposits, release in mill tailings, emissions from the nuclear industry, the combustion of coal and other fuels, and the use of phosphate fertilizers that contain uranium. The major source of exposure to uranium is food.

There are insufficient data regarding the carcinogenicity of uranium in humans and experimental animals. The guideline value for the chemical toxicity of uranium was therefore derived using a TDI approach. As no adequate long-term study was identified, the TDI was derived using the results of the most extensive short-term study conducted to date, in which uranium was administered in drinking-water to the most sensitive species and sex. In a 91-day study in rats, the LOAEL for degenerative lesions in the proximal convoluted tubule of the kidney in males was 0.96 mg of uranyl nitrate hexahydrate per litre, equivalent to 0.06 mg of uranium per kg of body weight per day.

A TDI of 0.6 $\mu\text{g}/\text{kg}$ of body weight per day was derived using the LOAEL of 60 $\mu\text{g}/\text{kg}$ of body weight per day and an uncertainty factor of 100 (for intra- and interspecies variation). Application of an additional uncertainty factor to account for the use of a LOAEL instead of a NOAEL is unnecessary because of the minimal severity of the lesions being reported. Moreover, no additional uncertainty factor for the length of the study (91 days) is required because the estimated half-life of uranium in the kidney is 15 days, and there is no indication that the severity of the renal lesions will be exacerbated following continued exposure.

This TDI yields a guideline value of 2 $\mu\text{g}/\text{litre}$ (rounded figure), assuming a 60-kg adult consuming 2 litres of drinking-water per day and a 10% allocation of the TDI to drinking-water.

There are several methods for removing uranium from drinking-water, although some have been tested only in the laboratory or on a pilot scale. Coagulation using ferric sulfate or aluminium sulfate at optimal pH and coagulation dosages can achieve 80-95% removal of uranium, whereas at least 99% removal can be achieved using lime softening, anion exchange resin, or reverse osmosis processes. In areas with high natural uranium levels, a value of 2 $\mu\text{g}/\text{litre}$ may be difficult to achieve with the treatment technology available. The guideline value is provisional because of these difficulties and because of limitations in the key study. It should be noted that several human studies are under way that may provide helpful additional data.

Source literature

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Organic constituents

Cyanobacterial toxins: microcystin-LR

The cyanobacteria, also known as blue-green algae, are a major group of bacteria that occur throughout the world. Freshwater cyanobacteria may accumulate in surface water supplies as "blooms" and may concentrate on the surface as blue-green "scums." Some species of cyanobacteria produce toxins, which are classified, according to their mode of action, as hepatotoxins (e.g. microcystins), neurotoxins (e.g. anatoxins), and skin irritants. The hepatotoxins are produced by various species within the genera *Microcystis*, *Anabaena*, *Oscillatoria*, *Nodularia*, *Nostoc*, *Cylindrospermopsis*, and *Umezakia*. Most hepatotoxins (all cyclic heptapeptides) are microcystins. The chemical structure of microcystins includes two variable amino acids and an unusual aromatic amino acid, ADDA (3-amino-9-methoxy-2,6,8-trimethyl-10-phenyldeca-4,6-dienoic acid), containing a substituted phenyldecadienoic acid. Microcystin-LR is a cyclic heptapeptide with a relative molecular mass of about 1000.

The growth of cyanobacteria and the formation of blooms are influenced by physical, chemical, and biological factors such as light intensity, temperature, water turbulence, presence of inorganic nitrogen and phosphorus nutrients, and pH.

The major route of human exposure to cyanobacterial toxins is the consumption of drinking-water. Some people are also exposed to cyanobacterial toxins through the consumption of certain algal food tablets.

Blue-green algae have been known to cause animal and human poisoning in lakes, ponds, and dugouts in various parts of the world for over 100 years. Cyanobacterial toxins have been implicated in human illness following consumption of water from certain municipal supplies in several countries, often after algal blooms had been treated with copper sulfate. In most cases, the cyanobacteria and sometimes the toxins involved have been identified, but the levels of toxin associated with illness have not been established with any certainty.

There are insufficient data to allow a guideline value to be derived for any cyanobacterial toxins other than microcystin-LR. A 13-week study in mice with microcystin-LR is considered the most suitable for the derivation of a guideline value for this toxin. In this study, a NOAEL of 40 $\mu\text{g}/\text{kg}$ of body weight per day was determined for liver pathology. A TDI of 0.04 $\mu\text{g}/\text{kg}$ of body weight per day can be calculated by applying an uncertainty factor of 1000 (100 for intra- and interspecies variation, 10 for limitations in the database, in particular lack of data on chronic toxicity and carcinogenicity) to the NOAEL. An allocation factor of 0.80 is used for the proportion of daily exposure arising from drinking-water, because there is little exposure from any other source or route. The resulting guideline value for total microcystin-LR (free plus cell-bound) is 1 $\mu\text{g}/\text{litre}$ (rounded figure) in drinking-water.

The guideline value thus calculated is supported by a 44-day study in which pigs were exposed, in their drinking-water, to an extract from *M. aeruginosa* containing microcystin-LR.

The guideline value of 1 $\mu\text{g}/\text{litre}$ is provisional as it covers only microcystin-LR, the database is limited, and new data for the toxicity of cyanobacterial toxins are being generated.

Edetic acid (EDTA)

Human exposure to EDTA arises directly from its use in food additives, medicines, and personal care and hygiene products. Exposure to EDTA from drinking-water is probably very small in comparison with that from other sources.

Once EDTA is present in the aquatic environment, its speciation will depend on the water quality and the presence of trace metals with which it can combine. The removal of EDTA from communal wastewater by biodegradation in sewage purification plants is very limited.

In 1973, JECFA established an ADI of 2.5 mg/kg of body weight for calcium disodium edetate as a food additive (1.9 mg/kg of body weight as the free acid). JECFA further evaluated the toxicological studies available on sodium iron EDTA in 1993; no further important information regarding the toxicity of EDTA and its calcium and sodium salts could be added to the 1973 evaluation. Concern has been expressed over the ability of EDTA to complex, and therefore reduce the availability of, zinc. However, this is of significance only at elevated doses substantially in excess of those encountered in the environment.

A guideline value for EDTA in drinking-water can be derived by allocating 1% of the ADI (1.9 mg/kg of body weight as the free acid) to drinking-water (because of the potential for significant exposure from food owing to use of EDTA as a food additive). Assuming a 60-kg adult ingesting 2 litres of drinking-water per day, the guideline value for EDTA (free acid) is therefore 600 µg/litre (rounded figure).

Polynuclear aromatic hydrocarbons (PAHs)

PAHs form a class of diverse organic compounds each containing two or more fused aromatic rings of carbon and hydrogen atoms. Most PAHs enter the environment via the atmosphere from a variety of combustion processes and pyrolysis sources. Owing to their low solubility and high affinity for particulate matter, they are not usually found in water in notable concentrations. The main source of PAH contamination in drinking-water is usually the coal-tar coating of drinking-water distribution pipes, used to protect the pipes from corrosion.

PAHs have been detected in a variety of foods as a result of the deposition of airborne PAHs, and in fish from contaminated waters. PAHs are also formed during some methods of food preparation, such as char-broiling, grilling, roasting, frying, or baking. For the general population, the major routes of exposure to PAHs are from food and ambient and indoor air. The use of open fires for heating and cooking may increase PAH exposure, especially in developing countries. Where there are elevated levels of contamination by coal-tar coatings of water pipes, PAH intake from drinking-water could be equal to or even exceed that from food.

Evidence that mixtures of PAHs are carcinogenic to humans comes primarily from occupational studies of workers following inhalation and dermal exposure. No data are available for humans for the oral route of exposure.

The guideline value for benzo[a]pyrene (BaP), one of the most carcinogenic PAHs, corresponding to an excess lifetime cancer risk of 10^{-5} , was estimated as 0.7 µg/litre in the *Guidelines for drinking-water quality*. This was based on an oral carcinogenicity study in mice and calculated using a two-stage birth - death mutation model, which incorporates variable dosing patterns and time of killing. Quantification of dose - response for tumours, on the basis of new studies in which the carcinogenicity of BaP was examined following oral administration in mice, but for which the number of dose groups was smaller, confirms this value. The guideline value of 0.7 µg/litre is therefore retained.

There are few data on the oral toxicity of PAHs other than BaP, particularly in drinking-water. Relative potencies of carcinogenic PAHs have been determined by comparison of data from dermal and other studies. The order of potencies is consistent, and this scheme therefore provides a useful indicator of PAH potency relative to BaP.

Fluoranthene (FA) is the most commonly detected PAH in drinking-water and is associated primarily with coal-tar linings of cast iron or ductile iron distribution pipes. In a 13-week gavage

study in mice, a NOAEL of 125 mg FA per kg of body weight per day was identified, based on increased serum glutamate pyruvate transaminase levels, kidney and liver pathology, and clinical and haematological changes. A conservative uncertainty factor of 10 000 (100 for interspecies and intraspecies variation, 10 for the use of a subchronic study and inadequate database, and 10 because of clear evidence of co-carcinogenicity with BaP in mouse skin-painting studies) gives a TDI of 0.0125 mg/kg of body weight per day. Assuming a 60-kg adult drinking 2 litres of water per day with an allocation of 1% of the TDI to water (because there is significant exposure from food), a health-based value of 4 µg/litre (rounded figure) can be calculated.

This health-based value is significantly above the concentrations normally found in drinking-water. Under usual conditions, therefore, the presence of FA in drinking-water does not represent a hazard to human health. For this reason, the establishment of a numerical guideline value for FA is not deemed necessary.

The presence of significant concentrations of BaP in drinking-water in the absence of very high concentrations of FA indicates the presence of coal-tar particles, which may arise from seriously deteriorating coal-tar pipe linings.

It is recommended that the use of coal-tar-based and similar materials for pipe linings and coatings on storage tanks be discontinued.

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Pesticides

Bentazone

Bentazone was evaluated in the second edition of the WHO *Guidelines for drinking-water quality*. A guideline value for bentazone of 30 µg/litre was based on an ADI of 0-0.1 mg/kg of body weight established by JMPR in 1991 (based upon haematological effects observed in a 2-year dietary study in rats), assuming a 60-kg person consuming 2 litres of drinking-water per day and allocating 1% of the ADI to drinking-water "to allow for uncertainties regarding dietary exposure." Bentazone is "moderately persistent in the environment" and therefore has the potential of being present in food.

Based on new information on the environmental behaviour of bentazone evaluated by the Core Assessment Group of JMP (Environment), bentazone does not seem to accumulate in the environment, and exposure from food is unlikely to be high. As a result, a 10% allocation of the ADI to drinking-water is appropriate for bentazone.

The new guideline value, based on this 10% allocation, is therefore 300 µg/litre.

Carbofuran

Carbofuran is used worldwide for many crops. Residues in treated crops are generally very low or not detectable. The physical and chemical properties of carbofuran and the few data on occurrence indicate that drinking-water from both groundwater and surface water sources is potentially the major route of exposure.

In 1996 carbofuran was re-evaluated by JMPR, and an ADI of 0-0.002 mg/kg of body weight was established on the basis of a NOAEL of 0.22 mg/kg of body weight per day in a short-term (4-week) study of acute (reversible) effects in dogs, the most sensitive species, using an uncertainty factor of 100. This 4-week study was conducted as an adjunct to a 13-week study in which inhibition of erythrocyte acetylcholinesterase activity was observed at the lowest dose of 0.43 mg/kg of body weight per day. Use of a 4-week study was considered appropriate because the NOAEL is based on a reversible acute effect. This NOAEL will also be protective for chronic effects.

On the basis of the ADI established by JMPR (2.2 µg/kg of body weight, if not rounded), and assuming a 60-kg person consuming 2 litres of drinking-water per day and an allocation of 10% of the ADI to drinking-water, a guideline value of 7 µg/litre (rounded figure) is obtained for carbofuran.

Cyanazine

Cyanazine is a member of the triazine family of herbicides. It is used as a pre- and post-emergence herbicide for the control of annual grasses and broadleaf weeds. It can be degraded

in soil and water by microorganisms and by hydrolysis, and has been detected in surface water and groundwater.

On the basis of the available mutagenicity data on cyanazine, evidence for genotoxicity is equivocal. Cyanazine causes mammary gland tumours in Sprague-Dawley rats but not in mice. The mechanism of mammary gland tumour development in Sprague-Dawley rats is currently under investigation and may prove to be hormonal. Cyanazine is also teratogenic in Fischer 344 rats at dose levels of 25 mg/kg of body weight per day and higher.

On the basis of hyperactivity in male rats in a 2-year toxicity/carcinogenicity study, a NOAEL of 0.198 mg/kg of body weight per day has been identified. By applying an uncertainty factor of 1000 (100 for interspecies and intraspecies variation and 10 for limited evidence of carcinogenicity), a TDI of 0.198 $\mu\text{g}/\text{kg}$ of body weight can be calculated. With an allocation of 10% of the TDI to drinking-water and assuming a 60-kg adult consuming 2 litres of drinking-water per day, the guideline value is 0.6 $\mu\text{g}/\text{litre}$ (rounded figure).

1,2-Dibromoethane

1,2-Dibromoethane is used as a lead scavenger in tetra-alkyl lead petrol and antiknock preparations and as a fumigant for soils, grains, and fruits. However, with the phasing-out of leaded petrol and of the use of 1,2-dibromoethane in agricultural applications in many countries, use of this substance has declined significantly. In addition to its continued use as a petrol additive in some countries, 1,2-dibromoethane is currently used principally as a solvent and as an intermediate in the chemical industry.

1,2-Dibromoethane has induced an increased incidence of tumours at several sites in all carcinogenicity bioassays identified in which rats or mice were exposed to the compound by gavage, ingestion in drinking-water, dermal application, and inhalation. However, many of these studies were characterized by high early mortality, limited histopathological examination, small group sizes, or use of only one exposure level. The substance acted as an initiator of liver foci in an initiation/promotion assay but did not initiate skin tumour development. 1,2-Dibromoethane was consistently genotoxic in *in-vitro* assays, although results in *in-vivo* assays were mixed. Biotransformation to active metabolites, which have been demonstrated to bind to DNA, is probably involved in the induction of tumours. Available data do not support the existence of a non-genotoxic mechanism of tumour induction. The available data thus indicate that 1,2-dibromoethane is a genotoxic carcinogen in rodents. Data on the potential carcinogenicity in humans are inadequate; however, it is likely that 1,2-dibromoethane is metabolized similarly in rodent species and in humans (although there may be varying potential for the production of active metabolites in humans, owing to genetic polymorphism). IARC classified 1,2-dibromoethane in Group 2A (the agent is probably carcinogenic to humans).

Although most of the available bioassays for 1,2-dibromoethane are limited, particularly those in which the compound was administered by ingestion, these studies can nevertheless be used to calculate approximate estimates of the carcinogenic potency of 1,2-dibromoethane. In view of the serious limitations of the studies, however, these estimates must be considered imprecise and, therefore, provisional.

Lifetime low-dose cancer risks can be calculated by linearized multistage modelling of the incidences of haemangiosarcomas and tumours in the stomach, liver, lung, and adrenal cortex (adjusted for the observed high early mortality, where appropriate, and corrected for the expected rate of increase in tumour formation in rodents in a standard bioassay of 104 weeks) of rats and/or mice exposed to 1,2-dibromoethane by gavage. The guideline value that corresponds to excess lifetime cancer risks (for various tumour types) of 10^{-5} is in the range 0.4-15 $\mu\text{g}/\text{litre}$.

Because of the serious limitations of the critical studies, the guideline value is considered provisional.

2,4-Dichlorophenoxyacetic acid (2,4-D)

The term 2,4-D is used here to refer to the free acid, 2,4-dichlorophenoxyacetic acid. Commercial 2,4-D products are marketed as the free acid, alkali and amine salts, and ester formulations. 2,4-D itself is chemically stable, but its esters are rapidly hydrolysed to the free acid.

2,4-D is a systemic herbicide used for control of broad-leaved weeds, including aquatic weeds. Impurities may be present in the technical product as a result of the manufacturing process. 2,4-D is rapidly biodegraded in the environment and levels in water are usually below 0.5 µg/litre. Residues of 2,4-D in food rarely exceed a few tens of µg/kg.

Epidemiological studies have suggested an association between exposure to chlorophenoxy herbicides, including 2,4-D, and two forms of cancer in humans: soft-tissue sarcomas and non-Hodgkin lymphoma. The results of these studies, however, are inconsistent; the associations found are weak, and conflicting conclusions have been reached by the investigators. Most of the studies did not provide information on exposure specifically to 2,4-D, and the risk was related to the general category of chlorophenoxy herbicides, a group that includes 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), which can be contaminated with dioxins. IARC has classified chlorophenoxy herbicides in Group 2B (the agent is possibly carcinogenic to humans) on the basis of limited evidence for carcinogenicity to humans and, for 2,4-D (and 2,4,5-T), inadequate evidence for carcinogenicity to animals.

JMPR re-evaluated 2,4-D in 1996 and concluded that it was not possible to assess its carcinogenic potential on the basis of the available epidemiological studies. JMPR established an ADI of 0-0.01 mg/kg of body weight for the sum of 2,4-D and its salts and esters, expressed as 2,4-D, on the basis of a NOAEL of 1 mg/kg of body weight per day in a 1-year study of toxicity in dogs and a 2-year study of toxicity and carcinogenicity in rats, using an uncertainty factor of 100.

The resulting guideline value of 30 µg/litre (using the ADI of 0.01 mg/kg of body weight and assuming a 60-kg person consuming 2 litres of drinking-water per day, and a 10% allocation to drinking-water) is therefore the same as in the 1993 *Guidelines for drinking-water quality*, but is based on the more recent toxicological evaluation conducted by JMPR. This guideline value applies to 2,4-D, as salts and esters of 2,4-D are rapidly hydrolysed to the free acid in water.

1,2-Dichloropropane (1,2-DCP)

1,2-DCP is used as an insecticide fumigant on grain and soil and to control peach-tree borers. It is also used as an intermediate in the production of perchloroethylene and other chlorinated products, and as a solvent. 1,2-DCP is relatively resistant to hydrolysis, is poorly adsorbed onto soil, and can migrate into groundwater.

1,2-DCP was evaluated by IARC in 1986 and 1987. The substance was classified in Group 3 (not classifiable as to its carcinogenicity to humans) on the basis of limited evidence for its carcinogenicity in experimental animals and the inability to evaluate its carcinogenicity in humans. Results from *in-vitro* assays for mutagenicity were mixed. The *in-vivo* studies, which were limited in number and design, were negative. In accordance with the IARC evaluation, the evidence from the long-term carcinogenicity studies in mice and rats was considered limited, and it was concluded that the use of a threshold approach for the toxicological evaluation of 1,2-DCP was appropriate.

A 13-week study in which male rats were given 1,2-DCP by gavage in corn oil for 5 days per week was considered to be the most appropriate study for the derivation of a guideline value. A LOAEL of 100 mg/kg of body weight (71.4 mg/kg of body weight per day when corrected for 5 days per week dosing) was observed for changes in haematological parameters. Using an uncertainty factor of 5000 (100 for interspecies and intraspecies variation, 10 for the use of a LOAEL instead of a NOAEL, and 5 for limitations of the database, including the limited data on *in-vivo* genotoxicity and use of a subchronic study), a TDI of 14 $\mu\text{g}/\text{kg}$ of body weight is derived. With an allocation of 10% of the TDI to drinking-water and assuming a 60-kg person consuming 2 litres of drinking-water per day, the provisional guideline value is 40 $\mu\text{g}/\text{litre}$ (rounded figure). The guideline value is considered to be provisional owing to the magnitude of the uncertainty factor and the fact that the database has not changed since the previous guideline value was derived.

Diquat

Diquat is a non-selective contact herbicide and crop desiccant. Because of its rapid degradation in water and strong adsorption onto sediments, diquat has rarely been found in drinking-water.

In 1993, JMPR established an ADI of 0-0.002 mg of diquat ion per kg of body weight based on a NOAEL of 0.19 mg of diquat ion per kg of body weight per day (based on cataract formation at the next higher dose) identified in a 2-year study in rats and using an uncertainty factor of 100. JMP examined issues relevant to the establishment of a guideline value for diquat in drinking-water and concluded that the ADI established by JMPR was relevant for the establishment of a drinking-water guideline value.

Assuming a 60-kg person consuming 2 litres of drinking-water per day and allocating 10% of the ADI established by JMPR (1.9 $\mu\text{g}/\text{kg}$ of body weight, if not rounded) to drinking-water, a health-based value of 6 $\mu\text{g}/\text{litre}$ (rounded figure) can be calculated for diquat ion.

However, the limit of detection of diquat in water is 1 $\mu\text{g}/\text{litre}$, and its practical quantification limit is about 10 $\mu\text{g}/\text{litre}$. A provisional guideline value of 10 $\mu\text{g}/\text{litre}$ is therefore established for diquat ion.

Glyphosate

Glyphosate is a broad-spectrum herbicide used in both agriculture and forestry and for aquatic weed control. Microbial biodegradation of glyphosate occurs in soil, aquatic sediment, and water, the major metabolite being aminomethylphosphonic acid (AMPA). Glyphosate is chemically stable in water and is not subject to photochemical degradation. The low mobility of glyphosate in soil indicates minimal potential for the contamination of groundwater. Glyphosate can, however, enter surface and subsurface waters after direct use near aquatic environments or by runoff or leaching from terrestrial applications.

In the Environmental Health Criteria monograph for glyphosate (WHO, 1994), a NOAEL of 175 mg/kg of body weight per day was identified in a teratogenicity study in rabbits and an uncertainty factor of 100 was considered appropriate for the derivation of an ADI for glyphosate. Using this ADI of 1.75 mg/kg of body weight and assuming a 60-kg person consuming 2 litres of drinking-water per day, a health-based value of 5 mg/litre (rounded figure) is obtained for an allocation of 10% of the ADI to drinking-water.

Because of the low toxicity of glyphosate, the health-based value derived for this herbicide is orders of magnitude higher than the concentrations normally found in drinking-water. Under usual conditions, therefore, the presence of glyphosate in drinking-water does not represent a hazard to human health, and the establishment of a numerical guideline value for glyphosate is not deemed necessary.

AMPA is the major metabolite of glyphosate. It was noted that most AMPA found in water comes from sources other than glyphosate degradation, and that AMPA is scheduled to be evaluated by JMPR.

Pentachlorophenol (PCP)

PCP and other chlorophenols are used primarily for protecting wood from fungal growth. Food is usually the major source of exposure to PCP unless there is a specific local chlorophenol contamination of drinking-water or exposure from log homes treated with PCP.

IARC classified PCP in Group 2B (the agent is possibly carcinogenic to humans) on the basis of inadequate evidence of carcinogenicity in humans but sufficient evidence in experimental animals. There is suggestive, although inconclusive, evidence of the carcinogenicity of PCP from epidemiological studies of populations exposed to mixtures that include PCP. Conclusive evidence of carcinogenicity has been obtained in one animal species (mice). Although there are notable variations in metabolism between experimental animals and humans, it was considered prudent to treat PCP as a potential carcinogen.

Adequate dose - response data for carcinogenicity are available only from toxicological studies in animals. On the basis of multistage modelling of tumour incidence in the mice bioassay, but recognizing that there are interspecies differences in metabolism, the concentration of PCP associated with a 10^{-5} excess lifetime cancer risk is similar to the current guideline value. The current provisional guideline value of 9 $\mu\text{g/litre}$ is therefore retained.

Terbutylazine (TBA)

TBA, a herbicide that belongs to the chlorotriazine family, is used in both pre- and post-emergence treatment of a variety of agricultural crops and in forestry. Degradation of TBA in natural water depends on the presence of sediments and biological activity. Concentrations found in water seldom exceed 0.2 $\mu\text{g/litre}$.

There is no evidence that TBA is carcinogenic or mutagenic. In a 2-year toxicity and carcinogenicity study in rats, a NOAEL of 0.22 mg/kg of body weight per day was identified for decreased body-weight gain at the next higher dose of 1 mg/kg of body weight per day. Using an uncertainty factor of 100 (for interspecies and intraspecies variation), the TDI is 2.2 $\mu\text{g/kg}$ of body weight.

Assuming a 60-kg person consuming 2 litres of drinking-water per day, and allocating 10% of the TDI to drinking-water, a guideline value of 7 $\mu\text{g/litre}$ (rounded figure) can be calculated for TBA in drinking-water.

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Disinfectant by-product

Chloroform

Chloroform is present in drinking-water largely as a result of formation from naturally occurring organic compounds during chlorination. Estimates of mean exposure from various media indicate that the general population is exposed to chloroform principally in food, drinking-water, and indoor air, in approximately equivalent amounts.

Most available evidence indicates that chloroform causes little, if any, gene mutation or other type of direct damage to DNA. Studies have indicated that liver tumours in mice are consistent with a threshold mechanism of induction; kidney tumours in rats may be similarly associated with a threshold mechanism, but the database is somewhat limited in this regard.

Several epidemiological studies of potential associations between ingestion of chlorinated drinking-water and colorectal and bladder cancer have been conducted. At present, the evidence for an association between exposure to trihalomethanes in drinking-water and rectal cancer must be considered inconclusive. There is no evidence of an increased risk of colon cancer, but studies have been conducted in areas where cumulative exposures are generally low. On the basis of available data it is not possible to conclude that the association between exposure to trihalomethanes and bladder cancer is causal, but observation of associations in well conducted studies where exposures were greatest cannot be lightly dismissed. Nevertheless, the evidence should be considered to be limited. Moreover, it is not possible to attribute excess bladder cancer cases to chloroform *per se*, although chloroform is generally the disinfectant by-product present at highest concentration in drinking-water.

A guideline value is therefore developed on the basis of a TDI for threshold effects. The most universally observed toxic effect of chloroform is damage to the centrilobular region of the liver. The severity of this effect per unit dose administered depends on the species, vehicle, and method by which the chloroform is administered. The lowest dose at which liver damage has been observed is 15 mg/kg of body weight per day administered in a toothpaste base to beagles over a period of 7.5 years. (Effects of lower doses were not examined.) Somewhat higher doses are required to produce hepatotoxic effects in other species. Effects in the proximal tubules of the kidney cortex have been observed in male mice of sensitive strains and in both male and female rats of several strains. Adverse histopathological effects have been observed at levels around 30 mg/kg of body weight per day in some studies in sensitive strains.

On the basis of the slight hepatotoxicity (increases in hepatic serum enzymes and fatty cysts) observed in beagle dogs ingesting 15 mg chloroform/kg of body weight per day in toothpaste for 7.5 years, and incorporating an uncertainty factor of 1000 (100 for interspecies and intraspecies variation and 10 for use of a LOAEL rather than a NOAEL and a subchronic study), a TDI of 13 µg/kg of body weight per day (corrected for 6 days/week dosing) is derived. Allocation of 50% of total intake to drinking-water is a reasonable default based on estimates indicating that the

general population is exposed to chloroform principally in food, drinking-water, and indoor air in approximately equivalent amounts and that most of the chloroform in indoor air is present as a result of volatilization from drinking-water. Assuming a 60-kg person consuming 2 litres of drinking-water per day, the guideline value is 200 $\mu\text{g/litre}$ (rounded figure).

It is noted that a drinking-water concentration for a 10^{-5} excess lifetime cancer risk, estimated on the basis of the default linearized multistage model for renal tumours in rats, is similar to the value developed on the basis of non-neoplastic effects.

It is cautioned that, where local circumstances require a choice to be made between meeting microbiological guidelines or guidelines for disinfection by-products such as chloroform, the microbiological quality must always take precedence. Efficient disinfection must *never* be compromised.

Source literature

Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits. Geneva, World Health Organization, 1994 (Environmental Health Criteria, No. 170).

Chloroform. In: *Some halogenated hydrocarbons.* Lyon, International Agency for Research on Cancer, 1979 (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 20).

Chloroform. Geneva, World Health Organization, 1994 (Environmental Health Criteria, No. 163).

Annex 1. List of participants in preparatory meetings

Coordinating Committee Meeting for the Updating of the WHO *Guidelines for drinking-water quality*, WHO, Geneva, 13-15 December 1995

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April 1997

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Annex 2. Tables of guideline values

The following tables present a summary of guideline values for chemicals in drinking-water. Individual values should not be used directly from the tables. The guideline values must be used and interpreted in conjunction with the information contained in the text.

Table A2.1. Chemicals of health significance in drinking-water

A. Inorganic constituents		
	Guideline value (mg/litre)	Remarks
boron	0.5 (P) ^a	
copper	2 (P)	Based on acute gastrointestinal effects
nickel	0.02 (P)	
nitrate (as NO ₃ ⁻)	50 (acute)	The sum of the ratio of the concentration of each to its respective (acute) guideline value should not exceed 1
nitrite (as NO ₂ ⁻)	3 (acute) 0.2 (P) (chronic)	
uranium	0.002 (P)	
B. Organic constituents		
	Guideline value (µg/litre)	Remarks
benzo[a]pyrene	0.7 ^b	For excess risk of 10 ⁻⁵
edetic acid (EDTA)	600	Applies to the free acid
microcystin-LR	1 (P)	Applies to total microcystin-LR (free plus cell-bound); data insufficient to derive guideline values for other cyanobacterial toxins
C. Pesticides		
	Guideline value (µg/litre)	Remarks
bentazone	300	
carbofuran	7	
cyanazine	0.6	
1,2-dibromoethane	0.4-15 ^b (P)	For excess risk of 10 ⁻⁵
2,4-dichlorophenoxyacetic acid (2,4-D)	30	
1,2-dichloropropane (1,2-DCP)	40 (P)	
diquat	10 (P)	
pentachlorophenol	9 ^b (P)	For excess risk of 10 ⁻⁵
terbutylazine (TBA)	7	
D. Disinfectant by-product		
	Guideline value (µg/litre)	Remarks
chloroform	200	

^a (P) Provisional guideline value. This term is used for constituents for which there is some evidence of a potential hazard but where the available information on health effects is limited; or where an uncertainty factor greater than 1000 has been used in the derivation of the tolerable daily intake (TDI). Provisional guideline values are also recommended: (1) for substances for which the calculated guideline value would be below the practical quantification level, or below the level that can be achieved through practical treatment methods; or (2) where disinfection is likely to result in the guideline value being exceeded.

^b For substances that are considered to be carcinogenic, the guideline value is the concentration in drinking-water associated with an excess lifetime cancer risk of 10^{-5} (one additional cancer per 100 000 of the population ingesting drinking-water containing the substance at the guideline value for 70 years). Concentrations associated with estimated excess lifetime cancer risks of 10^{-4} and 10^{-6} can be calculated by multiplying and dividing, respectively, the guideline value by 10.

In cases in which the concentration associated with an excess lifetime cancer risk of 10^{-5} is not feasible as a result of inadequate analytical or treatment technology, a provisional guideline value is recommended at a practicable level and the estimated associated excess lifetime cancer risk presented.

It should be emphasized that the guideline values for carcinogenic substances have been computed from hypothetical mathematical models that cannot be verified experimentally and that the values should be interpreted differently from TDI-based values because of the lack of precision of the models. At best, these values must be regarded as rough estimates of cancer risk. However, the models used are conservative and probably err on the side of caution. Moderate short-term exposure to levels exceeding the guideline value for carcinogens does not significantly affect the risk.

Table A2.2. Chemicals not of health significance at concentrations normally found in drinking-water

Chemical	Remarks
fluoranthene	U
glyphosate	U

U - It is unnecessary to recommend a health-based guideline value for these compounds because they are not hazardous to human health at concentrations normally found in drinking-water.

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Back cover

This Addendum to Volume 1 of the second edition of the *Guidelines for drinking-water quality* contains guideline values for a number of chemical substances that may be found in drinking-water, including inorganic substances (aluminium, boron, copper, nickel, nitrate, nitrite, and uranium), organic substances (edetic acid, microcystin-LR, polynuclear aromatic hydrocarbons), pesticides (bentazone, carbofuran, cyanazine, 1,2-dibromoethane, 2,4-dichlorophenoxyacetic acid, 1,2-dichloropropane, diquat, glyphosate, pentachlorophenol, and terbuthylazine), and a disinfectant by-product (chloroform).

Certain of these guideline values, established in the second edition of the *Guidelines*, have been reviewed and updated in the light of new scientific information. In addition, guidelines are included for a number of substances not covered by the second edition of the *Guidelines*.

It is emphasized that the guideline values recommended are not mandatory limits. Such limits should be set by national or regional authorities, using a risk-benefit approach and taking into consideration local environmental, social, economic, and cultural conditions.

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