of information on enteric adenoviruses is largely due to the fact that they are not detectable by conventional cell culture isolation.

Routes of exposure

Owing to the diverse epidemiology of the wide spectrum of HAds, exposure and infection are possible by a variety of routes. Person-to-person contact plays a major role in the transmission of illness; depending on the nature of illness, this can include faecal–oral, oral–oral and hand–eye contact transmission, as well as indirect transfer through contaminated surfaces or shared utensils. There have been numerous outbreaks associated with hospitals, military establishments, child care centres and schools. Symptoms recorded in most outbreaks were acute respiratory disease, keratoconjunctivitis and conjunctivitis. Outbreaks of gastroenteritis have also been reported. The consumption of contaminated food or water may be an important source of enteric illness, although there is no substantial evidence supporting this route of transmission. Eye infections may be contracted by the exposure of eyes to contaminated water, the sharing of towels at swimming pools or the sharing of goggles, as in the case of "shipyard eye." Confirmed outbreaks of adenovirus infections associated with water have been limited to pharyngitis and/or conjunctivitis, with exposure arising from use of swimming pools.

Significance in drinking-water

HAds have been shown to occur in substantial numbers in raw water sources and treated drinking-water supplies. In one study, the incidence of HAds in such waters was exceeded only by the group of enteroviruses among viruses detectable by PCR-based techniques. In view of their prevalence as an enteric pathogen and detection in water, contaminated drinking-water represents a likely but unconfirmed source of HAd infections. HAds are also considered important because they are exceptionally resistant to some water treatment and disinfection processes, notably UV light irradiation. HAds have been detected in drinking-water supplies that met accepted specifications for treatment, disinfection and conventional indicator organisms. Within a WSP, control measures to reduce potential risk from HAds should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove HAds will require validation. Drinking-water supplies should also be protected from contamination during distribution. Because of the high resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HAds in drinking-water supplies.

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11.2.2 Astroviruses

General description

Human and animal strains of astroviruses are single-stranded RNA viruses classified in the family Astroviridae. Astroviruses consist of a single-stranded RNA genome in a non-enveloped icosahedral capsid with a diameter of about 28 nm. In a proportion of the particles, a distinct surface star-shaped structure can be seen by electron microscopy. Eight different serotypes of human astroviruses (HAstVs) have been described. The most commonly identified is HAstV serotype 1. HAstVs can be detected in environmental samples using PCR techniques with or without initial cell culture amplification.

Human health effects

HAstVs cause gastroenteritis, predominantly diarrhoea, mainly in children under 5 years of age, although it has also been reported in adults. Seroprevalence studies showed that more than 80% of children between 5 and 10 years of age have antibodies against HAstVs. Occasional outbreaks in schools, nurseries and families have been reported. The illness is self-limiting, is of short duration and has a peak incidence in the winter. HAstVs are the cause of only a small proportion of reported gastroenteritis infections. However, the number of infections may be underestimated, since the illness is usually mild, and many cases will go unreported.

Source and occurrence

Infected individuals generally excrete large numbers of HAstVs in faeces; hence, the viruses will be present in sewage. HAstVs have been detected in water sources and in drinking-water supplies.

Routes of exposure

HAstVs are transmitted by the faecal–oral route. Person-to-person spread is considered the most common route of transmission, and clusters of cases are seen in child

care centres, paediatric wards, families, homes for the elderly and military establishments. Ingestion of contaminated food or water could also be important.

Significance in drinking-water

The presence of HAstVs in treated drinking-water supplies has been confirmed. Since the viruses are typically transmitted by the faecal–oral route, transmission by drinking-water seems likely, but has not been confirmed. HAstVs have been detected in drinking-water supplies that met accepted specifications for treatment, disinfection and conventional indicator organisms. Within a WSP, control measures to reduce potential risk from HAstVs should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove HAstVs will require validation. Drinking-water supplies should also be protected from contamination during distribution. Owing to the higher resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HAstVs in drinking-water supplies.

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11.2.3 Caliciviruses

General description

The family Caliciviridae consists of four genera of single-stranded RNA viruses with a non-enveloped capsid (diameter 35–40 nm), which generally displays a typical surface morphology resembling cup-like structures. Human caliciviruses (HuCVs) include the genera *Norovirus* (Norwalk-like viruses) and *Sapovirus* (Sapporo-like viruses). *Sapovirus* spp. demonstrate the typical calicivirus morphology and are called classical caliciviruses. Noroviruses generally fail to reveal the typical morphology and were in the past referred to as small round-structured viruses. The remaining two genera of the family contain viruses that infect animals other than humans. HuCVs cannot be propagated in available cell culture systems. The viruses were originally discovered by electron microscopy. Some *Norovirus* spp. can be detected by ELISA using antibodies raised against baculovirus-expressed *Norovirus* capsid proteins. Several reverse transcriptase PCR procedures have been described for the detection of HuCVs.

Human health effects

HuCVs are a major cause of acute viral gastroenteritis in all age groups. Symptoms include nausea, vomiting and abdominal cramps. Usually about 40% of infected individuals present with diarrhoea; some have fever, chills, headache and muscular pain. Since some cases present with vomiting only and no diarrhoea, the condition is also known as "winter vomiting disease." Infections by HuCVs induce a short-lived immunity. The symptoms are usually relatively mild and rarely last for more than 3 days. High attack rates in outbreaks indicate that the infecting dose is low.

Source and occurrence

HuCVs are excreted in faeces of infected individuals and will therefore be present in domestic wastewaters as well as faecally contaminated food and water, including drinking-water supplies.

Routes of exposure

The epidemiology of the disease indicates that person-to-person contact and the inhalation of contaminated aerosols and dust particles, as well as airborne particles of vomitus, are the most common routes of transmission. Drinking-water and a wide variety of foods contaminated with human faeces have been confirmed as major sources of exposure. Numerous outbreaks have been associated with contaminated drinking-water, ice, water on cruise ships and recreational waters. Shellfish harvested from sewage-contaminated waters have also been identified as a source of outbreaks.

Significance in drinking-water

Many HuCV outbreaks have been epidemiologically linked to contaminated drinking-water supplies. Within a WSP, control measures to reduce potential risk from HuCV should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove HuCV will require validation. Drinking-water supplies should also be protected from contamination during distribution. Owing to the higher resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HuCVs in drinking-water supplies.

Selected bibliography

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Monroe SS, Ando T, Glass R (2000) Introduction: Human enteric caliciviruses – An emerging pathogen whose time has come. *Journal of Infectious Diseases*, 181(Suppl. 2):S249–251.

11.2.4 Enteroviruses

General description

The genus *Enterovirus* is a member of the family Picornaviridae. This genus consists of 69 serotypes (species) that infect humans: poliovirus types 1–3, coxsackievirus types A1–A24, coxsackievirus types B1–B6, echovirus types 1–33 and the numbered enterovirus types EV68–EV73. Members of the genus are collectively referred to as enteroviruses. Other species of the genus infect animals other than humans – for instance, the bovine group of enteroviruses. Enteroviruses are among the smallest known viruses and consist of a single-stranded RNA genome in a non-enveloped icosahedral capsid with a diameter of 20–30 nm. Some members of the genus are readily isolated by cytopathogenic effect in cell cultures, notably poliovirus, coxsackievirus B, echovirus and enterovirus.

Human health effects

Enteroviruses are one of the most common causes of human infections. They have been estimated to cause about 30 million infections in the USA each year. The spectrum of diseases caused by enteroviruses is broad and ranges from a mild febrile illness to myocarditis, meningoencephalitis, poliomyelitis, herpangina, hand-foot-and-mouth disease and neonatal multi-organ failure. The persistence of the viruses in chronic conditions such as polymyositis, dilated cardiomyopathy and chronic fatigue syndrome has been described. Most infections, particularly in children, are asymptomatic, but still lead to the excretion of large numbers of the viruses, which may cause clinical disease in other individuals.

Source and occurrence

Enteroviruses are excreted in the faeces of infected individuals. Among the types of viruses detectable by conventional cell culture isolation, enteroviruses are generally the most numerous in sewage, water resources and treated drinking-water supplies. The viruses are also readily detected in many foods.

Routes of exposure

Person-to-person contact and inhalation of airborne viruses or viruses in respiratory droplets are considered to be the predominant routes of transmission of enteroviruses in communities. Transmission from drinking-water could also be important, but this has not yet been confirmed. Waterborne transmission of enteroviruses (coxsackievirus

A16 and B5) has been epidemiologically confirmed for only two outbreaks, and these were associated with children bathing in lake water in the 1970s.

Significance in drinking-water

Enteroviruses have been shown to occur in substantial numbers in raw water sources and treated drinking-water supplies. In view of their prevalence, drinking-water represents a likely, although unconfirmed, source of enterovirus infection. The limited knowledge on the role of waterborne transmission could be related to a number of factors, including the wide range of clinical symptoms, frequent asymptomatic infection, the diversity of serotypes and the dominance of person-to-person spread. Enteroviruses have been detected in drinking-water supplies that met accepted specifications for treatment, disinfection and conventional indicator organisms. Within a WSP, control measures to reduce potential risk from enteroviruses should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove enteroviruses will require validation. Drinking-water supplies should also be protected from contamination during distribution. Owing to the higher resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of enteroviruses in drinking-water supplies.

Selected bibliography

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11.2.5 Hepatitis A virus

General description

HAV is the only species of the genus *Hepatovirus* in the family Picornaviridae. The virus shares basic structural and morphological features with other members of the family, as described for enteroviruses. Human and simian HAVs are genotypically distinguishable. HAV cannot be readily detected or cultivated in conventional cell culture systems, and identification in environmental samples is based on the use of PCR techniques.

Human health effects

HAV is highly infectious, and the infecting dose is considered to be low. The virus causes the disease hepatitis A, commonly known as "infectious hepatitis." Like other members of the group enteric viruses, HAV enters the gastrointestinal tract by ingestion, where it infects epithelial cells. From here, the virus enters the bloodstream and reaches the liver, where it may cause severe damage to liver cells. In as many as 90%

of cases, particularly in children, there is little, if any, liver damage, and the infection passes without clinical symptoms and elicits lifelong immunity. In general, the severity of illness increases with age. The damage to liver cells results in the release of liver-specific enzymes such as aspartate aminotransferase, which are detectable in the bloodstream and used as a diagnostic tool. The damage also results in the failure of the liver to remove bilirubin from the bloodstream; the accumulation of bilirubin causes the typical symptoms of jaundice and dark urine. After a relatively long incubation period of 28–30 days on average, there is a characteristic sudden onset of illness, including symptoms such as fever, malaise, nausea, anorexia, abdominal discomfort and eventually jaundice. Although mortality is generally less than 1%, repair of the liver damage is a slow process that may keep patients incapacitated for 6 weeks or longer. This has substantial burden of disease implications. Mortality is higher in those over 50 years of age.

Source and occurrence

HAV occurs worldwide, but the prevalence of clinical disease has typical geographically based characteristics. HAV is excreted in faecal material of infected people, and there is strong epidemiological evidence that faecally contaminated food and water are common sources of the virus. In areas with poor sanitation, children are often infected at a very early age and become immune for life without clinical symptoms of disease. In areas with good sanitation, infection tends to occur later in life.

Routes of exposure

Person-to-person spread is probably the most common route of transmission, but contaminated food and water are important sources of infection. There is stronger epidemiological evidence for waterborne transmission of HAV than for any other virus. Foodborne outbreaks are also relatively common, with sources of infection including infected food handlers, shellfish harvested from contaminated water and contaminated produce. Travel of people from areas with good sanitation to those with poor sanitation provides a high risk of infection. Infection can also be spread in association with injecting and non-injecting drug use.

Significance in drinking-water

The transmission of HAV by drinking-water supplies is well established, and the presence of HAV in drinking-water constitutes a substantial health risk. Within a WSP, control measures to reduce potential risk from HAV should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove HAV will require validation. Drinking-water supplies should also be protected from contamination during distribution. Owing to the higher resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HAV in drinking-water supplies.

Selected bibliography

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WHO (2002) Enteric hepatitis viruses. In: *Guidelines for drinking-water quality*, 2nd ed. *Addendum: Microbiological agents in drinking water*. Geneva, World Health Organization, pp. 18–39.

11.2.6 Hepatitis E virus

General description

HEV consists of a single-stranded RNA genome in a non-enveloped icosahedral capsid with a diameter of 27–34 nm. HEV shares properties with a number of viruses, and classification is a challenge. At one stage, HEV was classified as a member of the family Caliciviridae, but most recently it has been placed in a separate family called hepatitis E-like viruses. There are indications of antigenic variation, and possibly even differences in serotypes of the virus, whereas human HAV consists of only one clearly defined serotype. HEV cannot be readily detected or cultivated in conventional cell culture systems, and identification in environmental samples is based on the use of PCR techniques.

Human health effects

HEV causes hepatitis that is in many respects similar to that caused by HAV. However, the incubation period tends to be longer (average 40 days), and infections typically have a mortality rate of up to 25% in pregnant women. In endemic regions, first infections are typically seen in young adults rather than young children. Despite evidence of antigenic variation, single infection appears to provide lifelong immunity to HEV. Global prevalence has a characteristic geographic distribution. HEV is endemic and causes clinical diseases in certain developing parts of the world, such as India, Nepal, central Asia, Mexico and parts of Africa. In many of these areas, HEV is the most important cause of viral hepatitis. Although seroprevalence can be high, clinical cases and outbreaks are rare in certain parts of the world, such as Japan, South Africa, the United Kingdom, North and South America, Australasia and central Europe. The reason for the lack of clinical cases in the presence of the virus is unknown.

Source and occurrence

HEV is excreted in faeces of infected people, and the virus has been detected in raw and treated sewage. Contaminated water has been associated with very large outbreaks. HEV is distinctive, in that it is the only enteric virus with a meaningful animal reservoir, including domestic animals, particularly pigs, as well as cattle, goats and even rodents.

Routes of exposure

Secondary transmission of HEV from cases to contacts and particularly nursing staff has been reported, but appears to be much less common than for HAV. The lower

level of person-to-person spread suggests that faecally polluted water could play a much more important role in the spread of HEV than of HAV. Waterborne outbreaks involving thousands of cases are on record. These include one outbreak in 1954 with approximately 40 000 cases in Delhi, India; one with more than 100 000 cases in 1986–1988 in the Xinjiang Uighar region of China; and one in 1991 with some 79 000 cases in Kanpur, India. Animal reservoirs may also serve as a route of exposure, but the extent to which humans contract HEV infection from animals remains to be elucidated.

Significance in drinking-water

The role of contaminated water as a source of HEV has been confirmed, and the presence of the virus in drinking-water constitutes a major health risk. There is no laboratory information on the resistance of the virus to disinfection processes, but data on waterborne outbreaks suggest that HEV may be as resistant as other enteric viruses. Within a WSP, control measures to reduce potential risk from HEV should focus on prevention of source water contamination by human and animal waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to remove HEV will require validation. Drinking-water supplies should also be protected from contamination during distribution. Due to the likelihood that the virus has a higher resistance to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HEV in drinking-water supplies.

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11.2.7 Rotaviruses and orthoreoviruses

General description

Members of the genus *Rotavirus* consist of a segmented double-stranded RNA genome in a non-enveloped icosahedral capsid with a diameter of 50–65 nm. This capsid is surrounded by a double-layered shell, giving the virus the appearance of a wheel – hence the name rotavirus. The diameter of the entire virus is about 80 nm. *Rotavirus* and *Orthoreovirus* are the two genera of the family Reoviridae typically associated with human infection. Orthoreoviruses are readily isolated by cytopathogenic effect on cell cultures. The genus *Rotavirus* is serologically divided into seven groups, A–G, each of which consists of a number of subgroups; some of these subgroups specifically infect

humans, whereas others infect a wide spectrum of animals. Groups A–C are found in humans, with group A being the most important human pathogens. Wild-type strains of rotavirus group A are not readily grown in cell culture, but there are a number of PCR-based detection methods available for testing environmental samples.

Human health effects

Human rotaviruses (HRVs) are the most important single cause of infant death in the world. Typically, 50–60% of cases of acute gastroenteritis of hospitalized children throughout the world are caused by HRVs. The viruses infect cells in the villi of the small intestine, with disruption of sodium and glucose transport. Acute infection has an abrupt onset of severe watery diarrhoea with fever, abdominal pain and vomiting; dehydration and metabolic acidosis may develop, and the outcome may be fatal if the infection is not appropriately treated. The burden of disease of rotavirus infections is extremely high. Members of the genus *Orthoreovirus* infect many humans, but they are typical "orphan viruses" and not associated with any meaningful disease.

Source and occurrence

HRVs are excreted by patients in numbers up to 10^{11} per gram of faeces for periods of about 8 days. This implies that domestic sewage and any environments polluted with the human faeces are likely to contain large numbers of HRVs. The viruses have been detected in sewage, rivers, lakes and treated drinking-water. Orthoreoviruses generally occur in wastewater in substantial numbers.

Routes of exposure

HRVs are transmitted by the faecal–oral route. Person-to-person transmission and the inhalation of airborne HRVs or aerosols containing the viruses would appear to play a much more important role than ingestion of contaminated food or water. This is confirmed by the spread of infections in children's wards in hospitals, which takes place much faster than can be accounted for by the ingestion of food or water contaminated by the faeces of infected patients. The role of contaminated water in transmission is lower than expected, given the prevalence of HRV infections and presence in contaminated water. However, occasional waterborne and foodborne outbreaks have been described. Two large outbreaks in China in 1982–1983 were linked to contaminated water supplies.

Significance in drinking-water

Although ingestion of drinking-water is not the most common route of transmission, the presence of HRVs in drinking-water constitutes a public health risk. There is some evidence that the rotaviruses are more resistant to disinfection than other enteric viruses. Within a WSP, control measures to reduce potential risk from HRVs should focus on prevention of source water contamination by human waste, followed by adequate treatment and disinfection. The effectiveness of treatment processes used to

remove HRVs will require validation. Drinking-water supplies should also be protected from contamination during distribution. Due to a higher resistance of the viruses to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index of the presence/absence of HRVs in drinking-water supplies.

Selected bibliography

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11.3 Protozoan pathogens

Protozoa and helminths are among the most common causes of infection and disease in humans and other animals. The diseases have a major public health and socioeconomic impact. Water plays an important role in the transmission of some of these pathogens. The control of waterborne transmission presents real challenges, because most of the pathogens produce cysts, oocysts or eggs that are extremely resistant to processes generally used for the disinfection of water and in some cases can be difficult to remove by filtration processes. Some of these organisms cause "emerging diseases." In the last 25 years, the most notable example of an emerging disease caused by a protozoan pathogen is cryptosporidiosis. Other examples are diseases caused by microsporidia and *Cyclospora*. As evidence for waterborne transmission of "emerging diseases" has been reported relatively recently, some questions about their epidemiology and behaviour in water treatment and disinfection processes remain to be elucidated. It would appear that the role of water in the transmission of this group of pathogens may increase substantially in importance and complexity as human and animal populations grow and the demands for potable drinking-water escalate.

Further information on emerging diseases is provided in *Emerging Issues in Water and Infectious Disease* (WHO, 2003) and associated texts.

11.3.1 Acanthamoeba

General description

Acanthamoeba spp. are free-living amoebae (10–50 µm in diameter) common in aquatic environments and one of the prominent protozoa in soil. The genus contains some 20 species, of which *A. castellanii*, *A. polyphaga* and *A. culbertsoni* are known to

be human pathogens. However, the taxonomy of the genus may change substantially when evolving molecular biological knowledge is taken into consideration. *Acanthamoeba* has a feeding, replicative trophozoite, which, under unfavourable conditions, such as an anaerobic environment, will develop into a dormant cyst that can withstand extremes of temperature (–20 to 56 °C), disinfection and desiccation.

Human health effects

Acanthamoeba culbertsoni causes granulomatous amoebic encephalitis (GAE), whereas *A. castellanii* and *A. polyphaga* are associated with acanthamoebic keratitis and acanthamoebic uveitis.

GAE is a multifocal, haemorrhagic and necrotizing encephalitis that is generally seen only in debilitated or immunodeficient persons. It is a rare but usually fatal disease. Early symptoms include drowsiness, personality changes, intense headaches, stiff neck, nausea, vomiting, sporadic low fevers, focal neurological changes, hemiparesis and seizures. This is followed by an altered mental status, diplopia, paresis, lethargy, cerebellar ataxia and coma. Death follows within a week to a year after the appearance of the first symptoms, usually as a result of bronchopneumonia. Associated disorders of GAE include skin ulcers, liver disease, pneumonitis, renal failure and pharyngitis.

Acanthamoebic keratitis is a painful infection of the cornea and can occur in healthy individuals, especially among contact lens wearers. It is a rare disease that may lead to impaired vision, permanent blindness and loss of the eye. The prevalence of antibodies to *Acanthamoeba* and the detection of the organism in the upper airways of healthy persons suggest that infection may be common with few apparent symptoms in the vast majority of cases.

Source and occurrence

The wide distribution of *Acanthamoeba* in the natural environment makes soil, airborne dust and water all potential sources. *Acanthamoeba* can be found in many types of aquatic environments, including surface water, tap water, swimming pools and contact lens solutions. Depending on the species, *Acanthamoeba* can grow over a wide temperature range in water, with the optimum temperature for pathogenic species being 30 °C. Trophozoites can exist and replicate in water while feeding on bacteria, yeasts and other organisms. Infections occur in most temperate and tropical regions of the world.

Routes of exposure

Acanthamoebic keratitis has been associated with soft contact lenses being washed with contaminated home-made saline solutions or contamination of the contact lens containers. Although the source of the contaminating organisms has not been established, tap water is one possibility. Warnings have been issued by a number of health agencies that only sterile water should be used to prepare wash solutions for contact

lenses. The mode of transmission of GAE has not been established, but water is not considered to be a source of infection. The more likely routes of transmission are via the blood from other sites of colonization, such as skin lesions or lungs.

Significance in drinking-water

Cases of acanthamoebic keratitis have been associated with drinking-water due to use of tap water in preparing solutions for washing contact lenses. Cleaning of contact lenses is not considered to be a normal use for tap water, and a higher-quality water may be required. Compared with *Cryptosporidium* and *Giardia*, *Acanthamoeba* is relatively large and is amenable to removal from raw water by filtration. Reducing the presence of biofilm organisms is likely to reduce food sources and growth of the organism in distribution systems, but the organism is highly resistant to disinfection. However, as normal uses of drinking-water lack significance as a source of infection, setting a health-based target for *Acanthamoeba* spp. is not warranted.

Selected bibliography

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Yagita K, Endo T, De Jonckheere JF (1999) Clustering of *Acanthamoeba* isolates from human eye infections by means of mitochondrial DNA digestion patterns. *Parasitology Research*, 85:284–289.

11.3.2 Balantidium coli

General description

Balantidium coli is a unicellular protozoan parasite with a length up to 200 µm, making it the largest of the human intestinal protozoa. The trophozoites are oval in shape and covered with cilia for motility. The cysts are 60–70 µm in length and resistant to unfavourable environmental conditions, such as pH and temperature extremes. *Balantidium coli* belongs to the largest protozoan group, the ciliates, with about 7200 species, of which only *B. coli* is known to infect humans.

Human health effects

Infections in humans are relatively rare, and most are asymptomatic. The trophozoites invade the mucosa and submucosa of the large intestine and destroy the host cells when multiplying. The multiplying parasites form nests and small abscesses that break down into oval, irregular ulcers. Clinical symptoms may include dysentery similar to amoebiasis, colitis, diarrhoea, nausea, vomiting, headache and anorexia. The infections are generally self-limiting, with complete recovery.

Source and occurrence

Humans seem to be the most important host of *B. coli*, and the organism can be detected in domestic sewage. Animal reservoirs, particularly swine, also contribute to

the prevalence of the cysts in the environment. The cysts have been detected in water sources, but the prevalence in tap water is unknown.

Routes of exposure

Transmission of *B. coli* is by the faecal–oral route, from person to person, from contact with infected swine or by consumption of contaminated water or food. One waterborne outbreak of balantidiasis has been reported. This outbreak occurred in 1971 when a drinking-water supply was contaminated with stormwater runoff containing swine faeces after a typhoon.

Significance in drinking-water

Although water does not appear to play an important role in the spread of this organism, one waterborne outbreak is on record. *Balantidium coli* is large and amenable to removal by filtration, but cysts are highly resistant to disinfection. Within a WSP, control measures to reduce potential risk from *B. coli* should focus on prevention of source water contamination by human and swine waste, followed by adequate treatment. Due to resistance to disinfection, *E. coli* (or, alternatively, thermotolerant coliforms) is not a reliable index for the presence/absence of *B. coli* in drinking-water supplies.

Selected bibliography

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11.3.3 Cryptosporidium

General description

Cryptosporidium is an obligate, intracellular, coccidian parasite with a complex life cycle including sexual and asexual replication. Thick-walled oocysts with a diameter of 4–6 µm are shed in faeces. The genus *Cryptosporidium* has about eight species, of which *C. parvum* is responsible for most human infections, although other species can cause illness. *Cryptosporidium* is one of the best examples of an "emerging disease"-causing organism. It was discovered to infect humans only in 1976, and waterborne transmission was confirmed for the first time in 1984.

Human health effects

Cryptosporidium generally causes a self-limiting diarrhoea, sometimes including nausea, vomiting and fever, which usually resolves within a week in normally healthy people, but can last for a month or more. Severity of cryptosporidiosis varies according to age and immune status, and infections in severely immunocompromised people can be life-threatening. The impact of cryptosporidiosis outbreaks is relatively high due to the large numbers of people that may be involved and the associated socioe-

conomic implications. The total cost of illness associated with the 1993 outbreak in Milwaukee, USA, has been estimated at US$96.2 million.

Source and occurrence

A large range of animals are reservoirs of *C. parvum*, but humans and livestock, particularly young animals, are the most significant source of human infectious organisms. Calves can excrete 10^{10} oocysts per day. Concentrations of oocysts as high as 14 000 per litre for raw sewage and 5800 per litre for surface water have been reported. Oocysts can survive for weeks to months in fresh water. *Cryptosporidium* oocysts have been detected in many drinking-water supplies. However, in most cases, there is little information about whether human infectious species were present. The currently available standard analytical techniques provide an indirect measure of viability and no indication of human infectivity. Oocysts also occur in recreational waters.

Routes of exposure

Cryptosporidium is transmitted by the faecal–oral route. The major route of infection is person-to-person contact. Other sources of infection include the consumption of contaminated food and water and direct contact with infected farm animals and possibly domestic pets. Contaminated drinking-water, recreational water and, to a lesser extent, food have been associated with outbreaks. In 1993, *Cryptosporidium* caused the largest waterborne outbreak of disease on record, when more than 400 000 people were infected by the drinking-water supply of Milwaukee, USA. The infectivity of *Cryptosporidium* oocysts is relatively high. Studies on healthy human volunteers revealed that ingestion of fewer than 10 oocysts can lead to infection.

Significance in drinking-water

The role of drinking-water in the transmission of *Cryptosporidium*, including in large outbreaks, is well established. Attention to these organisms is therefore important. The oocysts are extremely resistant to oxidizing disinfectants such as chlorine, but investigations based on assays for infectivity have shown that UV light irradiation inactivates oocysts. Within a WSP, control measures to reduce potential risk from *Cryptosporidium* should focus on prevention of source water contamination by human and livestock waste, adequate treatment and protection of water during distribution. Because of their relatively small size, the oocysts represent a challenge for removal by conventional granular media-based filtration processes. Acceptable removal requires well designed and operated systems. Membrane filtration processes that provide a direct physical barrier may represent a viable alternative for the effective removal of *Cryptosporidium* oocysts. Owing to the exceptional resistance of the oocysts to disinfectants, *E. coli* (or, alternatively, thermotolerant coliforms) cannot be relied upon as an index for the presence/absence of *Cryptosporidium* oocysts in drinking-water supplies.

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11.3.4 Cyclospora cayetanensis

General description

Cyclospora cayetanensis is a single-cell, obligate, intracellular, coccidian protozoan parasite, which belongs to the family Eimeriidae. It produces thick-walled oocysts of 8–10 µm in diameter that are excreted in the faeces of infected individuals. *Cyclospora cayetanensis* is considered an emerging waterborne pathogen.

Human health effects

Sporozoites are released from the oocysts when ingested and penetrate epithelial cells in the small intestine of susceptible individuals. Clinical symptoms of cyclosporiasis include watery diarrhoea, abdominal cramping, weight loss, anorexia, myalgia and occasionally vomiting and/or fever. Relapsing illness often occurs.

Source and occurrence

Humans are the only host identified for this parasite. The unsporulated oocysts pass into the external environment with faeces and undergo sporulation, which is complete in 7–12 days, depending on environmental conditions. Only the sporulated oocysts are infectious. Due to the lack of a quantification technique, there is limited information on the prevalence of *Cyclospora* in water environments. However, *Cyclospora* has been detected in sewage and water sources.

Routes of exposure

Cyclospora cayetanensis is transmitted by the faecal–oral route. Person-to-person transmission is virtually impossible, because the oocysts must sporulate outside the host to become infectious. The primary routes of exposure are contaminated water and food. The initial source of organisms in foodborne outbreaks has generally not

been established, but contaminated water has been implicated in several cases. Drinking-water has also been implicated as a cause of outbreaks. The first report was among staff of a hospital in Chicago, USA, in 1990. The infections were associated with drinking tap water that had possibly been contaminated with stagnant water from a rooftop storage reservoir. Another outbreak was reported from Nepal, where drinking-water consisting of a mixture of river and municipal water was associated with infections in 12 of 14 soldiers.

Significance in drinking-water

Transmission of the pathogens by drinking-water has been confirmed. The oocysts are resistant to disinfection and are not inactivated by chlorination practices generally applied in the production of drinking-water. Within a WSP, control measures that can be applied to manage potential risk from *Cyclospora* include prevention of source water contamination by human waste, followed by adequate treatment and protection of water during distribution. Owing to the resistance of the oocysts to disinfectants, *E. coli* (or, alternatively, thermotolerant coliforms) cannot be relied upon as an index of the presence/absence of *Cyclospora* in drinking-water supplies.

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11.3.5 Entamoeba histolytica

General description

Entamoeba histolytica is the most prevalent intestinal protozoan pathogen worldwide and belongs to the superclass Rhizopoda in the subphylum Sarcodina. *Entamoeba* has a feeding, replicative trophozoite (diameter 10–60 μm), which, under unfavourable conditions, will develop into a dormant cyst (diameter 10–20 μm). Infection is contracted by the ingestion of cysts. Recent studies with RNA and DNA probes demon-

strated genetic differences between pathogenic and non-pathogenic *E. histolytica*; the latter has been separated and reclassified as *E. dispar*.

Human health effects

About 85–95% of human infections with *E. histolytica* are asymptomatic. Acute intestinal amoebiasis has an incubation period of 1–14 weeks. Clinical disease results from the penetration of the epithelial cells in the gastrointestinal tract by the amoebic trophozoites. Approximately 10% of infected individuals present with dysentery or colitis. Symptoms of amoebic dysentery include diarrhoea with cramping, lower abdominal pain, low-grade fever and the presence of blood and mucus in the stool. The ulcers produced by the invasion of the trophozoites may deepen into the classic flask-shaped ulcers of amoebic colitis. *Entamoeba histolytica* may invade other parts of the body, such as the liver, lungs and brain, sometimes with fatal outcome.

Source and occurrence

Humans are the reservoir of infection, and there would not appear to be other meaningful animal reservoirs of *E. histolytica*. In the acute phase of infection, patients excrete only trophozoites that are not infectious. Chronic cases and asymptomatic carriers who excrete cysts are more important sources of infection and can discharge up to 1.5×10^7 cysts daily. *Entamoeba histolytica* can be present in sewage and contaminated water. Cysts may remain viable in suitable aquatic environments for several months at low temperature. The potential for waterborne transmission is greater in the tropics, where the carrier rate sometimes exceeds 50%, compared with more temperate regions, where the prevalence in the general population may be less than 10%.

Routes of exposure

Person-to-person contact and contamination of food by infected food handlers appear to be the most significant means of transmission, although contaminated water also plays a substantial role. Ingestion of faecally contaminated water and consumption of food crops irrigated with contaminated water can both lead to transmission of amoebiasis. Sexual transmission, particularly among male homosexuals, has also been documented.

Significance in drinking-water

The transmission of *E. histolytica* by contaminated drinking-water has been confirmed. The cysts are relatively resistant to disinfection and may not be inactivated by chlorination practices generally applied in the production of drinking-water. Within a WSP, control measures that can be applied to manage potential risk from *E. histolytica* include prevention of source water contamination by human waste, followed by adequate treatment and protection of water during distribution. Owing to the resistance of the oocysts to disinfectants, *E. coli* (or, alternatively, thermotolerant

coliforms) cannot be relied upon as an index of the presence/absence of *E. histolytica* in drinking-water supplies.

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11.3.6 Giardia intestinalis

General description

Giardia spp. are flagellated protozoa that parasitize the gastrointestinal tract of humans and certain animals. The genus *Giardia* consists of a number of species, but human infection (giardiasis) is usually assigned to *G. intestinalis*, also known as *G. lamblia* or *G. duodenalis*. *Giardia* has a relatively simple life cycle consisting of a flagellate trophozoite that multiplies in the gastrointestinal tract and an infective thick-walled cyst that is shed intermittently but in large numbers in faeces. The trophozoites are bilaterally symmetrical and ellipsoidal in shape. The cysts are ovoid in shape and 8–12 µm in diameter.

Human health effects

Giardia has been known as a human parasite for 200 years. After ingestion and excystation of cysts, the trophozoites attach to surfaces of the gastrointestinal tract. Infections in both children and adults may be asymptomatic. In day care centres, as many as 20% of children may carry *Giardia* and excrete cysts without clinical symptoms. The symptoms of giardiasis may result from damage caused by the trophozoites, although the mechanisms by which *Giardia* causes diarrhoea and intestinal malabsorption remain controversial. Symptoms generally include diarrhoea and abdominal cramps; in severe cases, however, malabsorption deficiencies in the small intestine may be present, mostly among young children. Giardiasis is self-limiting in most cases, but it may be chronic in some patients, lasting more than 1 year, even in otherwise healthy people. Studies on human volunteers revealed that fewer than 10 cysts constitute a meaningful risk of infection.

Source and occurrence

Giardia can multiply in a wide range of animal species, including humans, which excrete cysts into the environment. Numbers of cysts as high as 88 000 per litre in raw sewage and 240 per litre in surface water resources have been reported. These cysts are robust and can survive for weeks to months in fresh water. The presence of cysts in raw water sources and drinking-water supplies has been confirmed. However, there is no information on whether human infectious species were present. The currently available standard analytical techniques provide an indirect measure of viability and no indication of human infectivity. Cysts also occur in recreational waters and contaminated food.

Routes of exposure

By far the most common route of transmission of *Giardia* is person-to-person contact, particularly between children. Contaminated drinking-water, recreational water and, to a lesser extent, food have been associated with outbreaks. Animals have been implicated as a source of human infectious *G. intestinalis*, but further investigations are required to determine their role.

Significance in drinking-water

Waterborne outbreaks of giardiasis have been associated with drinking-water supplies for over 30 years; at one stage, *Giardia* was the most commonly identified cause of waterborne outbreaks in the USA. *Giardia* cysts are more resistant than enteric bacteria to oxidative disinfectants such as chlorine, but they are not as resistant as *Cryptosporidium* oocysts. The time required for 90% inactivation at a free chlorine residual of 1 mg/litre is about 25–30 min. Within a WSP, control measures that can be applied to manage potential risk from *Giardia* include prevention of source water contamination by human and animal waste, followed by adequate treatment and disinfection and protection of water during distribution. Owing to the resistance of the cysts to disinfectants, *E. coli* (or, alternatively, thermotolerant coliforms) cannot be relied upon as an index of the presence/absence of *Giardia* in drinking-water supplies.

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11.3.7 Isospora belli

General description

Isospora is a coccidian, single-celled, obligate parasite related to *Cryptosporidium* and *Cyclospora*. There are many species of *Isospora* that infect animals, but only *I. belli* is known to infect humans, the only known host for this species. *Isospora belli* is one of

the few coccidia that undergo sexual reproduction in the human intestine. Sporulated oocysts are ingested, and, after complete asexual and sexual life cycles in the mucosal epithelium of the upper small intestine, unsporulated oocysts are released in faeces.

Human health effects

Illness caused by *I. belli* is similar to that caused by *Cryptosporidium* and *Giardia*. About 1 week after ingestion of viable cysts, a low-grade fever, lassitude and malaise may appear, followed soon by mild diarrhoea and vague abdominal pain. The infection is usually self-limited after 1–2 weeks, but occasionally diarrhoea, weight loss and fever may last for 6 weeks to 6 months. Symptomatic isosporiasis is more common in children than in adults. Infection is often associated with immunocompromised patients, in whom symptoms are more severe and likely to be recurrent or chronic, leading to malabsorption and weight loss. Infections are usually sporadic and most common in the tropics and subtropics, although they also occur elsewhere, including industrialized countries. They have been reported from Central and South America, Africa and south-east Asia.

Source and occurrence

Unsporulated oocysts are excreted in the faeces of infected individuals. The oocysts sporulate within 1–2 days in the environment to produce the potentially infectious form of the organism. Few data are available on numbers of oocysts in sewage and raw and treated water sources. This is largely because sensitive and reliable techniques for the quantitative enumeration of oocysts in water environments are not available. Little is known about the survival of oocysts in water and related environments.

Routes of exposure

Poor sanitation and faecally contaminated food and water are the most likely sources of infection, but waterborne transmission has not been confirmed. The oocysts are less likely than *Cryptosporidium* oocysts or *Giardia* cysts to be transmitted directly from person to person, because freshly shed *I. belli* oocysts require 1–2 days in the environment to sporulate before they are capable of infecting humans.

Significance in drinking-water

The characteristics of *I. belli* suggest that illness could be transmitted by contaminated drinking-water supplies, but this has not been confirmed. No information is available on the effectiveness of water treatment processes for removal of *I. belli*, but it is likely that the organism is relatively resistant to disinfectants. It is considerably larger than *Cryptosporidium* and should be easier to remove by filtration. Within a WSP, control measures that can be applied to manage potential risk from *I. belli* include prevention of source water contamination by human waste, followed by adequate treatment and disinfection and protection of water during distribution. Owing to the likely resistance of the oocysts to disinfectants, *E. coli* (or, alternatively, thermotolerant coliforms)

cannot be relied upon as an index of the presence/absence of *I. belli* in drinking-water supplies.

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11.3.8 Microsporidia

General description

The term "microsporidia" is a non-taxonomic designation commonly used to describe a group of obligate intracellular protozoa belonging to the phylum Microspora. More than 100 microsporidial genera and almost 1000 species have been identified. Infections occur in every major animal group, including vertebrates and invertebrates. A number of genera have been implicated in human infections, including *Enterocytozoon*, *Encephalitozoon* (including *Septata*), *Nosema*, *Pleistophora*, *Vittaforma* and *Trachipleistophora*, as well as a collective group of unclassified microsporidia referred to as microsporidium. Microsporidia are among the smallest eukaryotes. They produce unicellular spores with a diameter of 1.0–4.5 µm and a characteristic coiled polar filament for injecting the sporoplasm into a host cell to initiate infection. Within an infected cell, a complex process of multiplication takes place, and new spores are produced and released in faeces, urine, respiratory secretions or other body fluids, depending on the type of species and the site of infection.

Human health effects

Microsporidia are emerging human pathogens identified predominantly in persons with AIDS, but their ability to cause disease in immunologically normal hosts has been recognized. Reported human infections are globally dispersed and have been documented in persons from all continents. The most common clinical manifestation in AIDS patients is a severe enteritis involving chronic diarrhoea, dehydration and weight loss. Prolonged illness for up to 48 months has been reported. Infections in the general population are less pronounced. *Enterocytozoon* infection generally appears to be limited to intestinal enterocytes and biliary epithelium. *Encephalitozoon* spp. infect a variety of cells, including epithelial and endothelial cells, fibroblasts, kidney tubule cells, macrophages and possibly other cell types. Unusual complications include keratoconjunctivitis, myositis and hepatitis.

Source and occurrence

The sources of microsporidia infecting humans are uncertain. Spores are likely to be excreted in faeces and are also excreted in urine and respiratory secretions. Due to the lack of a quantification technique, there is limited information on the prevalence of microsporidia spores in water environments. However, microsporidia have been detected in sewage and water sources. Indications are that their numbers in raw sewage may be similar to those of *Cryptosporidium* and *Giardia*, and they may survive in certain water environments for many months. Certain animals, notably swine, may serve as a host for human infectious species.

Routes of exposure

Little is known about transmission of microsporidia. Person-to-person contact and ingestion of spores in water or food contaminated with human faeces or urine are probably important routes of exposure. A waterborne outbreak of microsporidiosis has been reported involving about 200 cases in Lyon, France, during the summer of 1995. However, the source of the organism and faecal contamination of the drinking-water supply were not demonstrated. Transmission by the inhalation of airborne spores or aerosols containing spores seems possible. The role of animals in transmission to humans remains unclear. Epidemiological and experimental studies in mammals suggest that *Encephalitozoon* spp. can be transmitted transplacentally from mother to offspring. No information is available on the infectivity of the spores. However, in view of the infectivity of spores of closely related species, the infectivity of microsporidia may be high.

Significance in drinking-water

Waterborne transmission has been reported, and infection arising from contaminated drinking-water is plausible but unconfirmed. Little is known about the response of microsporidia to water treatment processes. One study has suggested that the spores may be susceptible to chlorine. The small size of the organism is likely to make them difficult to remove by filtration processes. Within a WSP, control measures that can be applied to manage potential risk from microsporidia include prevention of source water contamination by human and animal waste, followed by adequate treatment and disinfection and protection of water during distribution. Owing to the lack of information on sensitivity of infectious species of microsporidia to disinfection, the reliability of *E. coli* (or, alternatively, thermotolerant coliforms) as an index for the presence/absence of these organisms from drinking-water supplies is unknown.

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11.3.9 Naegleria fowleri

General description

Naegleria are free-living amoeboflagellates distributed widely in the environment. There are several species of *Naegleria*, of which *N. fowleri* is the primary infectious species. *Naegleria* spp. exist as a trophozoite, a flagellate and a cyst stage. The trophozoite (10–20 μm) moves by eruptive pseudopod formation feeding on bacteria and reproduces by binary fission. The trophozoite can transform into a flagellate stage with two anterior flagella. The flagellate does not divide but reverts to the trophozoite stage. Under adverse conditions, the trophozoite transforms into a circular cyst (7–15 μm), which is resistant to unfavourable conditions.

Human health effects

Naegleria fowleri causes primary amoebic meningoencephalitis (PAM) in healthy individuals. The amoeba enters the brain by penetrating the olfactory mucosa and cribiform plate. The disease is acute, and patients often die within 5–10 days and before the infectious agent can be diagnosed. Treatment is difficult. Although the infection is rare, new cases are reported every year.

Source and occurrence

Naegleria fowleri is thermophilic and grows well at temperatures up to 45 °C. It occurs naturally in fresh water of suitable temperature, and prevalence is only indirectly related to human activity, inasmuch as such activity may modify temperature or promote bacterial (food source) production. The pathogen has been reported from many countries, usually associated with thermally polluted water environments such as geothermal water or heated swimming pools. However, the organism has been detected in drinking-water supplies, particularly where water temperature can exceed 25–30 °C. Water is the only known source of infection. The first cases of amoebic meningitis were diagnosed in 1965 in Australia and Florida. Since that time, about 100 cases of PAM have been reported throughout the world.

Routes of exposure

Infection with *N. fowleri* is almost exclusively contracted by exposure of the nasal passages to contaminated water. Infection is predominantly associated with recreational use of water, including swimming pools and spas, as well as surface waters naturally heated by the sun, industrial cooling waters and geothermal springs. In a limited number of cases, a link to recreational water exposure is lacking. The occurrence of PAM is highest during hot summer months, when many people engage in water recreation and when the temperature of water is conducive to growth of the organism. Consumption of contaminated water or food and person-to-person spread have not been reported as routes of transmission.

Significance in drinking-water

Naegleria fowleri has been detected in drinking-water supplies. Although unproven, a direct or indirect role of drinking-water-derived organisms – for example, through use of drinking-water in swimming pools – is possible. Any water supply that seasonally exceeds 30 °C or that continually exceeds 25 °C can potentially support the growth of *N. fowleri*. In such cases, a periodic prospective study would be valuable. Free chlorine or monochloramine residuals in excess of 0.5 mg/litre have been shown to control *N. fowleri*, providing the disinfectant persists through the water distribution system. In addition to maintaining persistent disinfectant residuals, other control measures aimed at limiting the presence of biofilm organisms will reduce food sources and hence growth of the organism in distribution systems. Owing to the environmental nature of this amoeba, *E. coli* (or, alternatively, thermotolerant coliforms) cannot be relied upon as an index for the presence/absence of *N. fowleri* in drinking-water supplies.

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11.3.10 Toxoplasma gondii

General description

Many species of *Toxoplasma* and *Toxoplasma*-like organisms have been described, but it would appear that *T. gondii* is the only human infectious species. *Toxoplasma gondii* is a coccidian parasite, and the cat is the definitive host. Only cats harbour the parasite in the intestinal tract, where sexual reproduction takes place. The actively multiplying asexual form in the human host is an obligate, intracellular parasite (diameter 3–6 μm) called a tachyzoite. A chronic phase of the disease develops as the tachyzoites transform into slowly replicating bradyzoites, which eventually become cysts in the host tissue. In the natural cycle, mice and rats containing infective cysts are eaten by cats, which host the sexual stage of the parasite. The cyst wall is digested, and bradyzoites penetrate epithelial cells of the small intestine. Several generations of intracellular multiplication lead to the development of micro- and macrogametes. Fertilization of the latter leads to the development of oocysts that are excreted in faeces as early as 5 days after a cat has ingested the cysts. Oocysts require 1–5 days to sporulate in the environment. Sporulated oocysts and tissue-borne cysts can both cause infections in susceptible hosts.

Human health effects

Toxoplasmosis is usually asymptomatic in humans. In a small percentage of cases, flu-like symptoms, lymphadenopathy and hepatosplenomegaly present 5–23 days after the ingestion of cysts or oocysts. Dormant cysts, formed in organ tissue after primary infection, can be reactivated when the immune system becomes suppressed, producing disseminated disease involving the central nervous system and lungs and leading to severe neurological disorders or pneumonia. When these infection sites are involved, the disease can be fatal in immunocompromised patients. Congenital toxoplasmosis is mostly asymptomatic, but can produce chorioretinitis, cerebral calcifications, hydrocephalus, severe thrombocytopenia and convulsions. Primary infection during early pregnancy can lead to spontaneous abortion, stillbirth or fetal abnormality.

Source and occurrence

Toxoplasmosis is found worldwide. Estimates indicate that in many parts of the world, 15–30% of lamb and pork meat is infected with cysts. The prevalence of oocyst-shedding cats may be 1%. By the third decade of life, about 50% of the European population is infected, and in France this proportion is close to 80%. *Toxoplasma gondii* oocysts may occur in water sources and supplies contaminated with the faeces of infected cats. Due to a lack of practical methods for the detection of *T. gondii* oocysts, there is little information on the prevalence of the oocysts in raw and treated water supplies. Details on the survival and behaviour of the oocysts in water environments are also not available. However, qualitative evidence of the presence of oocysts in faecally polluted water has been reported, and results suggest that *T. gondii*

oocysts may be as resistant to unfavourable conditions in water environments as the oocysts of related parasites.

Routes of exposure

Both *T. gondii* oocysts that sporulate after excretion by cats and tissue-borne cysts are potentially infectious. Humans can become infected by ingestion of oocysts excreted by cats by direct contact or through contact with contaminated soil or water. Two outbreaks of toxoplasmosis have been associated with consumption of contaminated water. In Panama, creek water contaminated by oocysts from jungle cats was identified as the most likely source of infection, while in 1995, an outbreak in Canada was associated with a drinking-water reservoir being contaminated by excreta from domestic or wild cats. A study in Brazil during 1997–1999 identified the consumption of unfiltered drinking-water as a risk factor for *T. gondii* seropositivity. More commonly, humans contract toxoplasmosis through the consumption of undercooked or raw meat and meat products containing *T. gondii* cysts. Transplacental infection also occurs.

Significance in drinking-water

Contaminated drinking-water has been identified as a source of toxoplasmosis outbreaks. Little is known about the response of *T. gondii* to water treatment processes. The oocysts are larger than *Cryptosporidium* oocysts and should be amenable to removal by filtration. Within a WSP, control measures to manage potential risk from *T. gondii* should be focused on prevention of source water contamination by wild and domesticated cats. If necessary, the organisms can be removed by filtration. Owing to the lack of information on sensitivity of *T. gondii* to disinfection, the reliability of *E. coli* (or, alternatively, thermotolerant coliforms) as an indicator for the presence/absence of these organisms in drinking-water supplies is unknown.

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11.4 Helminth pathogens

The word "helminth" comes from the Greek word meaning "worm" and refers to all types of worms, both free-living and parasitic. The major parasitic worms are classi-

fied primarily in the phylum Nematoda (roundworms) and the phylum Platyhelminthes (flatworms including trematodes). Helminth parasites infect a large number of people and animals worldwide. For most helminths, drinking-water is not a significant route of transmission. There are two exceptions: *Dracunculus medinensis* (guinea worm) and *Fasciola* spp. (*F. hepatica* and *F. gigantica*) (liver flukes). Dracunculiasis and fascioliasis both require intermediate hosts to complete their life cycles but are transmitted through drinking-water by different mechanisms. Other helminthiases can be transmitted through water contact (schistosomiasis) or are associated with the use of untreated wastewater in agriculture (ascariasis, trichuriasis, hookworm infections and strongyloidiasis) but are not usually transmitted through drinking-water.

11.4.1 Dracunculus medinensis

Dracunculus medinensis, commonly known as "guinea worm," belongs to the phylum Nematoda and is the only nematode associated with significant transmission by drinking-water.

The eradication of guinea worm infection from the world by 1995 was a target of the International Drinking Water Supply and Sanitation Decade (1981–1990), and the World Health Assembly formally committed itself to this goal in 1991. The Dracunculus Eradication Programme has achieved a massive reduction in the number of cases. There were an estimated 3.3 million cases in 1986, 625 000 cases in 1990 and fewer than 60 000 cases in 2002, with the majority occurring in Sudan. Dracunculiasis is restricted to a central belt of countries in sub-Saharan Africa.

General description

The *D. medinensis* worms inhabit the cutaneous and subcutaneous tissues of infected individuals, the female reaching a length of up to 700 mm, and the male 25 mm. When the female is ready to discharge larvae (embryos), its anterior end emerges from a blister or ulcer, usually on the foot or lower limb, and releases large numbers of rhabditiform larvae when the affected part of the body is immersed in water. The larvae can move about in water for approximately 3 days and during that time can be ingested by many species of *Cyclops* (cyclopoid Copepoda, Crustacea). The larvae penetrate into the haemocoelom, moult twice and are infective to a new host in about 2 weeks. If the *Cyclops* (0.5–2.0 mm) are swallowed in drinking-water, the larvae are released in the stomach, penetrate the intestinal and peritoneal walls and inhabit the subcutaneous tissues.

Human health effects

The onset of symptoms occurs just prior to the local eruption of the worm. The early manifestations of urticaria, erythema, dyspnoea, vomiting, pruritus and giddiness are of an allergic nature. In about 50% of cases, the whole worm is extruded in a few weeks; the lesion then heals rapidly, and disability is of limited duration. In the

remaining cases, however, complications ensue, and the track of the worm becomes secondarily infected, leading to a severe inflammatory reaction that may result in abscess formation with disabling pain that lasts for months. Mortality is extremely rare, but permanent disability can result from contractures of tendons and chronic arthritis. The economic impact can be substantial. One study reported an 11% annual reduction in rice production from an area of eastern Nigeria, at a cost of US$20 million.

Source and occurrence

Infection with guinea worm is geographically limited to a central belt of countries in sub-Saharan Africa. Drinking-water containing infected *Cyclops* is the only source of infection with *Dracunculus*. The disease typically occurs in rural areas where piped water supplies are not available. Transmission tends to be highly seasonal, depending on changes in water sources. For instance, transmission is highest in the early rainy season in a dry savannah zone of Mali with under 800 mm annual rainfall but in the dry season in the humid savannah area of southern Nigeria with over 1300 mm annual rainfall. The eradication strategy combines a variety of interventions, including integrated surveillance systems, intensified case containment measures, provision of safe water and health education.

Routes of exposure

The only route of exposure is the consumption of drinking-water containing *Cyclops* spp. carrying infectious *Dracunculus* larvae.

Significance in drinking-water

Dracunculus medinensis is the only human parasite that may be eradicated in the near future by the provision of safe drinking-water. Infection can be prevented by a number of relatively simple control measures. These include intervention strategies to prevent the release of *D. medinensis* larvae from female worms in infected patients into water and control of *Cyclops* spp. in water resources by means of fish. Prevention can also be achieved through the provision of boreholes and safe wells. Wells and springs should be surrounded by cement curbings, and bathing and washing in these waters should be avoided. Other control measures include filtration of water carrying infectious *Dracunculus* larvae through a fine mesh cloth to remove *Cyclops* spp. or inactivation of *Cyclops* spp. in drinking-water by treatment with chlorine.

Selected bibliography

Cairncross S, Muller R, Zagaria N (2002) Dracunculiasis (guinea worm disease) and the eradication initiative. *Clinical Microbiology Reviews*, 15:223–246.

Hopkins DR, Ruiz-Tiben E (1991) Strategies for dracunculiasis eradication. *Bulletin of the World Health Organization*, 69:533–540.

11.4.2 Fasciola spp.

Fascioliasis is caused by two trematode species of the genus *Fasciola*: *F. hepatica*, present in Europe, Africa, Asia, the Americas and Oceania, and *F. gigantica*, mainly distributed in Africa and Asia. Human fascioliasis was considered a secondary zoonotic disease until the mid-1990s. In most regions, fascioliasis is a foodborne disease. However, the discovery of floating metacercariae in hyperendemic regions (including the Andean Altiplano region in South America) indicates that drinking-water may be a significant transmission route for fascioliasis in certain locations.

General description

The life cycle of *F. hepatica* and *F. gigantica* takes about 14–23 weeks and requires two hosts. The life cycle comprises four phases. In the first phase, the definitive host ingests metacercariae. The metacercariae excyst in the intestinal tract and then migrate to the liver and bile ducts. After 3–4 months, the flukes attain sexual maturity and produce eggs, which are excreted into the bile and intestine. Adult flukes can live for 9–14 years in the host. In the second phase, the eggs are excreted by the human or animal. Once in fresh water, a miracidium develops inside. In the third phase, miracidia penetrate a snail host and develop into cercaria, which are released into the water. In the fourth and final phase, cercaria swim for a short period of time until they reach a suitable attachment site (aquatic plants), where they encyst to form metacercariae, which become infective within 24 h. Some metacercariae do not attach to plants but remain floating in the water.

Human health effects

The parasites inhabit the large biliary passages and the gall-bladder. Disease symptoms are different for the acute and chronic phases of the infection. The invasive or acute phase may last from 2 to 4 months and is characterized by symptoms such as dyspepsia, nausea and vomiting, abdominal pain and a high fever (up to 40 °C). Anaemia and allergic responses (e.g., pruritis, urticaria) may also occur. In children, the acute infection can be accompanied by severe symptoms and sometimes causes death. The obstructive or chronic phase (after months to years of infection) may be characterized by painful liver enlargement and in some cases obstructive jaundice, chest pains, loss of weight and cholelithiasis. The most important pathogenic sequelae are hepatic lesions and fibrosis and chronic inflammation of the bile ducts. Immature flukes may deviate during migration, enter other organs and cause ectopic fascioliasis in a range of subcutaneous tissues. Fascioliasis can be treated with triclabendazole.

Source and occurrence

Human cases have been increasing in 51 countries on five continents. Estimates of the numbers of humans with fascioliasis range from 2.4 to 17 million people or even higher, depending on unquantified prevalence in many African and Asian countries.

Analysis of the geographical distribution of human cases shows that the correlation between animal and human fascioliasis occurs only at a basic level. High prevalences in humans are not necessarily related to areas where fascioliasis is a great veterinary problem. Major health problems associated with fascioliasis occur in Andean countries (Bolivia, Peru, Chile, Ecuador), the Caribbean (Cuba), northern Africa (Egypt), Near East (Iran and neighbouring countries) and western Europe (Portugal, France and Spain).

Routes of exposure

Humans can contract fascioliasis when they ingest infective metacercariae by eating raw aquatic plants (and, in some cases, terrestrial plants, such as lettuce, irrigated with contaminated water), drinking contaminated water, using utensils washed in contaminated water or eating raw liver infected with immature flukes.

Significance in drinking-water

Water is often cited as a human infection source. In the Bolivian Altiplano, 13% of metacercariae isolates are floating. Untreated drinking-water in hyperendemic regions often contains floating metacercariae; for example, a small stream crossing in the Altiplano region of Bolivia contained up to 7 metacercariae per 500 ml. The importance of fascioliasis transmission through water is supported by indirect evidence. There are significant positive associations between liver fluke infection and infection by other waterborne protozoans and helminths in Andean countries and in Egypt. In many human hyperendemic areas of the Americas, people do not have a history of eating watercress or other water plants. In the Nile Delta region, people living in houses with piped water had a higher infection risk. Metacercariae are likely to be resistant to chlorine disinfection but should be removed by various filtration processes. For example, in Tiba, Egypt, human prevalence was markedly decreased after filtered water was supplied to specially constructed washing units.

Selected bibliography

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11.5 Toxic cyanobacteria

More detailed information on toxic cyanobacteria is available in the supporting document *Toxic Cyanobacteria in Water* (see section 1.3).

General description

Cyanobacteria are photosynthetic bacteria that share some properties with algae. Notably, they possess chlorophyll-a and liberate oxygen during photosynthesis. The first species to be recognized were blue-green in colour; hence, a common term for these organisms is blue-green algae. However, owing to the production of different pigments, there are a large number that are not blue-green, and they can range in colour from blue-green to yellow-brown and red. Most cyanobacteria are aerobic phototrophs, but some exhibit heterotrophic growth. They may grow as separate cells or in multicellular filaments or colonies. They can be identified by their morphology to genus level under a microscope. Some species form surface blooms or scums, while others stay mixed in the water column or are bottom dwelling (benthic). Some cyanobacteria possess the ability to regulate their buoyancy via intracellular gas vacuoles, and some species can fix elemental nitrogen dissolved in water. The most notable feature of cyanobacteria in terms of public health impact is that a range of species can produce toxins.

Human health effects

Many cyanobacteria produce potent toxins, as shown in Table 11.1. Cyanobacterial toxins are also discussed in section 8.5.6. Each toxin has specific properties, with distinct concerns including liver damage, neurotoxicity and tumour promotion. Acute symptoms reported after exposure include gastrointenstinal disorders, fever and irritations of the skin, ears, eyes, throat and respiratory tract. Cyanobacteria do not multiply in the human body and hence are not infectious.

Source and occurrence

Cyanobacteria are widespread and found in a diverse range of environments, including soils, seawater and, most notably, freshwater environments. Some environmental conditions, including sunlight, warm weather, low turbulence and high nutrient levels, can promote growth. Depending on the species, this may result in greenish discol-

Table 11.1 Cyanotoxins produced by cyanobacteria

Toxic species	Cyanotoxin
Potentially *Anabaena* spp.	Anatoxin-a(S), anatoxin-a, microcystins, saxitoxins
Anabaenopsis millenii	Microcystins
Aphanizomenon spp.	Anatoxin-a, saxitoxins, cylindrospermopsin
Cylindrospermum spp.	Cylindrospermopsin, saxitoxins, anatoxin-a
Lyngbya spp.	Saxitoxins, lyngbyatoxins
Microcystis spp.	Microcystins, anatoxin-a (minor amounts)
Nodularia spp.	Nodularins
Nostoc spp.	Microcystins
Oscillatoria spp.	Anatoxin-a, microcystins
Planktothrix spp.	Anatoxin-a, homoanatoxin-a, microcystins
Raphidiopsis curvata	Cylindrospermopsin
Umezakia natans	Cylindrospermopsin

oration of water due to a high density of suspended cells and, in some cases, the formation of surface scums. Such cell accumulations may lead to high toxin concentrations.

Routes of exposure

Potential health concerns arise from exposure to the toxins through ingestion of drinking-water, during recreation, through showering and potentially through consumption of algal food supplement tablets. Repeated or chronic exposure is the primary concern for many of the cyanotoxins; in some cases, however, acute toxicity is more important (e.g., lyngbyatoxins and the neurotoxins saxitoxin and anatoxin). Human fatalities have occurred through use of inadequately treated water containing high cyanotoxin levels for renal dialysis. Dermal exposure may lead to irritation of the skin and mucous membranes and to allergic reactions.

Significance in drinking-water

Cyanobacteria occur in low cell density in most surface waters. However, in suitable environmental conditions, high-density "blooms" can occur. Eutrophication (increased biological growth associated with increased nutrients) can support the development of cyanobacterial blooms (see also section 8.5.6).

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Lahti K et al. (2001) Occurrence of microcystins in raw water sources and treated drinking water of Finnish waterworks. *Water Science and Technology*, 43:225–228.

11.6 Indicator and index organisms

Owing to issues relating to complexity, cost and timeliness of obtaining results, testing for specific pathogens is generally limited to validation, where monitoring is used to determine whether a treatment or other process is effective in removing target organisms. Very occasionally, pathogen testing may be performed to verify that a specific treatment or process has been effective. However, microbial testing included as part of operational and verification (including surveillance) monitoring is usually limited to that for indicator organisms, either to measure the effectiveness of control measures or as an index of faecal pollution.

The concept of using indicator organisms as signals of faecal pollution is a well established practice in the assessment of drinking-water quality. The criteria determined for such indicators were that they should not be pathogens themselves and should:

— be universally present in faeces of humans and animals in large numbers;
— not multiply in natural waters;
— persist in water in a similar manner to faecal pathogens;
— be present in higher numbers than faecal pathogens;
— respond to treatment processes in a similar fashion to faecal pathogens; and
— be readily detected by simple, inexpensive methods.

These criteria reflect an assumption that the same indicator organism could be used as both an index of faecal pollution and an indicator of treatment/process efficacy. However, it has become clear that one indicator cannot fulfil these two roles. Increased attention has focused on shortcomings of traditional indicators, such as *E. coli*, as surrogates for enteric viruses and protozoa, and alternative indicators of these pathogens, such as bacteriophages and bacterial spores, have been suggested. In addition, greater reliance is being placed on parameters that can be used as indicators for the effectiveness of treatments and processes designed to remove faecal pathogens, including bacteria, viruses, protozoa and helminths.

It is important to distinguish between microbial testing undertaken to signal the presence of faecal pathogens or alternatively to measure the effectiveness of treatments/processes. As a first step, the separate terms *index* and *indicator* have been proposed, whereby:

— an *index organism* is one that points to the presence of pathogenic organisms – for example, as an index of faecal pathogens; and
— an *indicator organism* is one that is used to measure the effectiveness of a process – for example, a process indicator or disinfection indicator.

These terms can also be applied to non-microbial parameters; hence, turbidity can be used a filtration indicator.

Further discussion on index and indicator organisms is contained in the supporting document *Assessing Microbial Safety of Drinking Water* (see section 1.3).

11.6.1 Total coliform bacteria

General description

Total coliform bacteria include a wide range of aerobic and facultatively anaerobic, Gram-negative, non-spore-forming bacilli capable of growing in the presence of relatively high concentrations of bile salts with the fermentation of lactose and production of acid or aldehyde within 24 h at 35–37 °C. *Escherichia coli* and thermotolerant coliforms are a subset of the total coliform group that can ferment lactose at higher temperatures (see section 11.6.2). As part of lactose fermentation, total coliforms produce the enzyme β-galactosidase. Traditionally, coliform bacteria were regarded as belonging to the genera *Escherichia*, *Citrobacter*, *Klebsiella* and *Enterobacter*, but the group is more heterogeneous and includes a wider range of genera, such as *Serratia* and *Hafnia*. The total coliform group includes both faecal and environmental species.

Indicator value

Total coliforms include organisms that can survive and grow in water. Hence, they are not useful as an index of faecal pathogens, but they can be used as an indicator of treatment effectiveness and to assess the cleanliness and integrity of distribution systems and the potential presence of biofilms. However, there are better indicators for these purposes. As a disinfection indicator, the test for total coliforms is far slower and less reliable than direct measurement of disinfectant residual. In addition, total coliforms are far more sensitive to disinfection than are enteric viruses and protozoa. HPC measurements detect a wider range of microorganisms and are generally considered a better indicator of distribution system integrity and cleanliness.

Source and occurrence

Total coliform bacteria (excluding *E. coli*) occur in both sewage and natural waters. Some of these bacteria are excreted in the faeces of humans and animals, but many coliforms are heterotrophic and able to multiply in water and soil environments. Total coliforms can also survive and grow in water distribution systems, particularly in the presence of biofilms.

Application in practice

Total coliforms are generally measured in 100-ml samples of water. A variety of relatively simple procedures are available based on the production of acid from lactose or the production of the enzyme β-galactosidase. The procedures include membrane filtration followed by incubation of the membranes on selective media at 35–37 °C and counting of colonies after 24 h. Alternative methods include most probable number procedures using tubes or micro-titre plates and P/A tests. Field test kits are available.

Significance in drinking-water

Total coliforms should be absent immediately after disinfection, and the presence of these organisms indicates inadequate treatment. The presence of total coliforms in distribution systems and stored water supplies can reveal regrowth and possible biofilm formation or contamination through ingress of foreign material, including soil or plants.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

Grabow WOK (1996) Waterborne diseases: Update on water quality assessment and control. *Water SA*, 22:193–202.

Sueiro RA et al. (2001) Evaluation of Coli-ID and MUG Plus media for recovering *Escherichia coli* and other coliform bacteria from groundwater samples. *Water Science and Technology*, 43:213–216.

11.6.2 Escherichia coli and thermotolerant coliform bacteria

General description

Total coliform bacteria that are able to ferment lactose at 44–45 °C are known as thermotolerant coliforms. In most waters, the predominant genus is *Escherichia*, but some types of *Citrobacter*, *Klebsiella* and *Enterobacter* are also thermotolerant. *Escherichia coli* can be differentiated from the other thermotolerant coliforms by the ability to produce indole from tryptophan or by the production of the enzyme β-glucuronidase. *Escherichia coli* is present in very high numbers in human and animal faeces and is rarely found in the absence of faecal pollution, although there is some evidence for growth in tropical soils. Thermotolerant coliform species other than *E. coli* can include environmental organisms.

Indicator value

Escherichia coli is considered the most suitable index of faecal contamination. In most circumstances, populations of thermotolerant coliforms are composed predominantly of *E. coli*; as a result, this group is regarded as a less reliable but acceptable index of faecal pollution. *Escherichia coli* (or, alternatively, thermotolerant coliforms) is the first organism of choice in monitoring programmes for verification, including surveillance of drinking-water quality. These organisms are also used as disinfection indicators, but testing is far slower and less reliable than direct measurement of disinfectant residual. In addition, *E. coli* is far more sensitive to disinfection than are enteric viruses and protozoa.

Source and occurrence

Escherichia coli occurs in high numbers in human and animal faeces, sewage and water subject to recent faecal pollution. Water temperatures and nutrient conditions present in drinking-water distribution systems are highly unlikely to support the growth of these organisms.

Application in practice

Escherichia coli (or, alternatively, thermotolerant coliforms) are generally measured in 100-ml samples of water. A variety of relatively simple procedures are available based on the production of acid and gas from lactose or the production of the enzyme β-glucuronidase. The procedures include membrane filtration followed by incubation of the membranes on selective media at 44–45 °C and counting of colonies after 24 h. Alternative methods include most probable number procedures using tubes or microtitre plates and P/A tests, some for volumes of water larger than 100 ml. Field test kits are available.

Significance in drinking-water

The presence of *E. coli* (or, alternatively, thermotolerant coliforms) provides evidence of recent faecal contamination, and detection should lead to consideration of further action, which could include further sampling and investigation of potential sources such as inadequate treatment or breaches in distribution system integrity.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

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Grabow WOK (1996) Waterborne diseases: Update on water quality assessment and control. *Water SA*, 22:193–202.

Sueiro RA et al. (2001) Evaluation of Coli-ID and MUG Plus media for recovering *Escherichia coli* and other coliform bacteria from groundwater samples. *Water Science and Technology*, 43:213–216.

11.6.3 Heterotrophic plate counts

A substantial review of the use of HPC is available (Bartram et al., 2003).

General description

HPC measurement detects a wide spectrum of heterotrophic microorganisms, including bacteria and fungi, based on the ability of the organisms to grow on rich growth media, without inhibitory or selective agents, over a specified incubation period and at a defined temperature. The spectrum of organisms detected by HPC testing includes organisms sensitive to disinfection processes, such as coliform bacteria; organisms resistant to disinfection, such as spore formers; and organisms that rapidly proliferate in treated water in the absence of residual disinfectants. The tests detect only a small proportion of the microorganisms that are present in water. The population recovered will differ according to the method and conditions applied. Although standard methods have been developed, there is no single universal HPC measurement. A range of media is available, incubation temperatures used vary from 20 °C to 37 °C and incubation periods range from a few hours to 7 days or more.

Indicator value

The test has little value as an index of pathogen presence but can be useful in operational monitoring as a treatment and disinfectant indicator, where the objective is to keep numbers as low as possible. In addition, HPC measurement can be used in assessing the cleanliness and integrity of distribution systems and the presence of biofilms.

Source and occurrence

Heterotrophic microorganisms include both members of the natural (typically non-hazardous) microbial flora of water environments and organisms present in a range of pollution sources. They occur in large numbers in raw water sources. The actual organisms detected by HPC tests vary widely between locations and between consecutive samples. Some drinking-water treatment processes, such as coagulation and sedimentation, reduce the number of HPC organisms in water. However, the organisms proliferate in other treatment processes, such as biologically active carbon and sand filtration. Numbers of HPC organisms are reduced significantly by disinfection practices, such as chlorination, ozonation and UV light irradiation. However, in practice, none of the disinfection processes sterilizes water; under suitable conditions, such as the absence of disinfectant residuals, HPC organisms can grow rapidly. HPC organisms can grow in water and on surfaces in contact with water as biofilms. The principal determinants of growth or "regrowth" are temperature, availability of nutrients, including assimilable organic carbon, lack of disinfectant residual and stagnation.

Application in practice

No sophisticated laboratory facilities or highly trained staff are required. Results on simple aerobically incubated agar plates are available within hours to days, depending on the characteristics of the procedure used.

Significance in drinking-water

After disinfection, numbers would be expected to be low; for most uses of HPC test results, however, actual numbers are of less value than changes in numbers at particular locations. In distribution systems, increasing numbers can indicate a deterioration in cleanliness, possibly stagnation and the potential development of biofilms. HPC can include potentially "opportunistic" pathogens such as *Acinetobacter*, *Aeromonas*, *Flavobacterium*, *Klebsiella*, *Moraxella*, *Serratia*, *Pseudomonas* and *Xanthomonas*. However, there is no evidence of an association of any of these organisms with gastrointestinal infection through ingestion of drinking-water in the general population.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

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11.6.4 Intestinal enterococci

General description

Intestinal enterococci are a subgroup of the larger group of organisms defined as faecal streptococci, comprising species of the genus *Streptococcus*. These bacteria are Gram-positive and relatively tolerant of sodium chloride and alkaline pH levels. They are facultatively anaerobic and occur singly, in pairs or as short chains. Faecal streptococci including intestinal enterococci all give a positive reaction with Lancefield's Group D antisera and have been isolated from the faeces of warm-blooded animals. The subgroup intestinal enterococci consists of the species *Enterococcus faecalis*, *E. faecium*, *E. durans* and *E. hirae.* This group was separated from the rest of the faecal streptococci because they are relatively specific for faecal pollution. However, some intestinal enterococci isolated from water may occasionally also originate from other habitats, including soil, in the absence of faecal pollution.

Indicator value

The intestinal enterococci group can be used as an index of faecal pollution. Most species do not multiply in water environments. The numbers of intestinal enterococci in human faeces are generally about an order of magnitude lower than those of *E. coli.* Important advantages of this group are that they tend to survive longer in water environments than *E. coli* (or thermotolerant coliforms), are more resistant to drying and are more resistant to chlorination. Intestinal enterococci have been used in testing of raw water as an index of faecal pathogens that survive longer than *E. coli* and in drinking-water to augment testing for *E. coli*. In addition, they have been used to test water quality after repairs to distribution systems or after new mains have been laid.

Source and occurrence

Intestinal enterococci are typically excreted in the faeces of humans and other warm-blooded animals. Some members of the group have also been detected in soil in the absence of faecal contamination. Intestinal enterococci are present in large numbers in sewage and water environments polluted by sewage or wastes from humans and animals.

Application in practice

Enterococci are detectable by simple, inexpensive cultural methods that require basic bacteriology laboratory facilities. Commonly used methods include membrane filtration with incubation of membranes on selective media and counting of colonies after incubation at 35–37 °C for 48 h. Other methods include a most probable number technique using micro-titre plates where detection is based on the ability of intestinal enterococci to hydrolyse 4-methyl-umbelliferyl-β-D-glucoside in the presence of thallium acetate and nalidixic acid within 36 h at 41 °C.

Significance in drinking-water

The presence of intestinal enterococci provides evidence of recent faecal contamination, and detection should lead to consideration of further action, which could include further sampling and investigation of potential sources such as inadequate treatment or breaches in distribution system integrity.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

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Pinto B et al. (1999) Characterization of "faecal streptococci" as indicators of faecal pollution and distribution in the environment. *Letters in Applied Microbiology*, 29:258–263.

11.6.5 Clostridium perfringens

General description

Clostridium spp. are Gram-positive, anaerobic, sulfite-reducing bacilli. They produce spores that are exceptionally resistant to unfavourable conditions in water environments, including UV irradiation, temperature and pH extremes, and disinfection processes, such as chlorination. The characteristic species of the genus, *C. perfringens*, is a member of the normal intestinal flora of 13–35% of humans and other warm-blooded animals. Other species are not exclusively of faecal origin. Like *E. coli*, *C. perfringens* does not multiply in most water environments and is a highly specific indicator of faecal pollution.

Indicator value

In view of the exceptional resistance of *C. perfringens* spores to disinfection processes and other unfavourable environmental conditions, *C. perfringens* has been proposed as an index of enteric viruses and protozoa in treated drinking-water supplies. In addition, *C. perfringens* can serve as an index of faecal pollution that took place previously and hence indicate sources liable to intermittent contamination. *Clostridium perfringens* is not recommended for routine monitoring, as the exceptionally long survival times of its spores are likely to far exceed those of enteric pathogens, including viruses and protozoa. *Clostridium perfringens* spores are smaller than protozoan (oo)cysts and may be useful indicators of the effectiveness of filtration processes. Low numbers in

some source waters suggest that use of *C. perfringens* spores for this purpose may be limited to validation of processes rather than routine monitoring.

Source and occurrence

Clostridium perfringens and its spores are virtually always present in sewage. The organism does not multiply in water environments. *Clostridium perfringens* is present more often and in higher numbers in the faeces of some animals, such as dogs, than in the faeces of humans and less often in the faeces of many other warm-blooded animals. The numbers excreted in faeces are normally substantially lower than those of *E. coli*.

Application in practice

Vegetative cells and spores of *C. perfringens* are usually detected by membrane filtration techniques in which membranes are incubated on selective media under strict anaerobic conditions. These detection techniques are not as simple and inexpensive as those for other indicators, such as *E. coli* and intestinal enterococci.

Significance in drinking-water

The presence of *C. perfringens* in drinking-water can be an index of intermittent faecal contamination. Potential sources of contamination should be investigated. Filtration processes designed to remove enteric viruses or protozoa should also remove *C. perfringens*. Detection in water immediately after treatment should lead to investigation of filtration plant performance.

Selected bibliography

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Payment P, Franco E (1993) *Clostridium perfringens* and somatic coliphages as indicators of the efficiency of drinking-water treatment for viruses and protozoan cysts. *Applied and Environmental Microbiology*, 59:2418–2424.

11.6.6 Coliphages

General description

Bacteriophages (phages) are viruses that use only bacteria as hosts for replication. Coliphages use *E. coli* and closely related species as hosts and hence can be released

by these bacterial hosts into the faeces of humans and other warm-blooded animals. Coliphages used in water quality assessment are divided into the major groups of somatic coliphages and F-RNA coliphages. Differences between the two groups include the route of infection.

Somatic coliphages initiate infection by attaching to receptors permanently located on the cell wall of hosts. They replicate more frequently in the gastrointestinal tract of warm-blooded animals but can also replicate in water environments. Somatic coliphages consist of a wide range of phages (members of the phage families Myoviridae, Siphoviridae, Podoviridae and Microviridae) with a spectrum of morphological types.

F-RNA coliphages initiate infection by attaching to fertility (F-, sex) fimbriae on *E. coli* hosts. These F-fimbriae are produced only by bacteria carrying the fertility (F-) plasmid. Since F-fimbriae are produced only in the logarithmic growth phase at temperatures above 30 °C, F-RNA phages are not likely to replicate in environments other than the gastrointestinal tract of warm-blooded animals. F-RNA coliphages comprise a restricted group of closely related phages, which belong to the family Leviviridae, and consist of a single-stranded RNA genome and an icosahedral capsid that is morphologically similar to that of picornaviruses. F-RNA coliphages have been divided into serological types I–IV, which can be identified as genotypes by molecular techniques such as gene probe hybridization. Members of groups I and IV have to date been found exclusively in animal faeces, and group III in human faeces. Group II phages have been detected in human faeces and no animal faeces other than about 28% of porcine faeces. This specificity, which is not fully understood, offers a potential tool to distinguish between faecal pollution of human and animal origin under certain conditions and limitations.

Indicator value

Phages share many properties with human viruses, notably composition, morphology, structure and mode of replication. As a result, coliphages are useful models or surrogates to assess the behaviour of enteric viruses in water environments and the sensitivity to treatment and disinfection processes. In this regard, they are superior to faecal bacteria. However, there is no direct correlation between numbers of coliphages and numbers of enteric viruses. In addition, coliphages cannot be absolutely relied upon as an index for enteric viruses. This has been confirmed by the isolation of enteric viruses from treated and disinfected drinking-water supplies that yielded negative results in conventional tests for coliphages.

F-RNA coliphages provide a more specific index of faecal pollution than somatic phages. In addition, F-RNA coliphages are better indicators of the behaviour of enteric viruses in water environments and their response to treatment and disinfection processes than are somatic coliphages. This has been confirmed by studies in which the behaviour and survival of F-RNA coliphages, somatic phages, faecal bacteria and enteric viruses have been compared. Available data indicate that the specificity of F-

RNA serogroups (genotypes) for human and animal excreta may prove useful in the distinction between faecal pollution of human and animal origin. However, there are shortcomings and conflicting data that need to be resolved, and the extent to which this tool can be applied in practice remains to be elucidated. Due to the limitations of coliphages, they are best used in laboratory investigations, pilot trials and possibly validation testing. They are not suitable for operational or verification (including surveillance) monitoring.

Source and occurrence

Coliphages are excreted by humans and animals in relatively low numbers. As a result of their respective modes of replication and host specificity, somatic coliphages are generally excreted by most humans and animals, whereas F-RNA coliphages are excreted by a variable and generally lower percentage of humans and animals. Available data indicate that in some communities, F-RNA phages are detectable in 10% of human, 45% of bovine, 60% of porcine and 70% of poultry faecal specimens. Somatic coliphages have been found to generally outnumber F-RNA phages in water environments by a factor of about 5 and cytopathogenic human viruses by a factor of about 500, although these ratios vary considerably. Sewage contains somatic coliphages in numbers of the order of 10^6–10^8 per litre; in one study, slaughterhouse wastewater was found to contain somatic coliphages in numbers up to 10^{10} per litre. There are indications that they may multiply in sewage, and somatic coliphages may multiply in natural water environments using saprophytic hosts. Somatic phages and F-RNA phages have been detected in numbers up to 10^5 per litre in lake and river water.

Application in practice

Somatic coliphages are detectable by relatively simple and inexpensive plaque assays, which yield results within 24 h. Plaque assays for F-RNA coliphages are not quite as simple, because the culture of host bacteria has to be in the logarithmic growth phase at a temperature above 30 °C to ensure that F-fimbriae are present. Plaque assays using large petri dishes have been designed for the quantitative enumeration of plaques in 100-ml samples, and P/A tests have been developed for volumes of water of 500 ml or more.

Significance in drinking-water

Since coliphages typically replicate in the gastrointestinal tract of humans and warm-blooded animals, their presence in drinking-water provides an index of faecal pollution and hence the potential presence of enteric viruses and possibly also other pathogens. The presence of coliphages in drinking-water also indicates shortcomings in treatment and disinfection processes designed to remove enteric viruses. F-RNA coliphages provide a more specific index for faecal pollution. The absence of coliphages from treated drinking-water supplies does not confirm the absence of pathogens such as enteric viruses and protozoan parasites.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

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Storey MV, Ashbolt NJ (2001) Persistence of two model enteric viruses (B40-8 and MS-2 bacteriophages) in water distribution pipe biofilms. *Water Science and Technology*, 43:133–138.

11.6.7 Bacteroides fragilis phages

General description

The bacterial genus *Bacteroides* inhabits the human gastrointestinal tract in greater numbers than *E. coli*. Faeces can contain 10^9–10^{10} *Bacteroides* per gram compared with 10^6–10^8 *E. coli* per gram. *Bacteroides* are rapidly inactivated by environmental oxygen levels, but *Bacteroides* bacteriophages are resistant to unfavourable conditions. Two groups of *B. fragilis* phages are used as indicators in water quality assessment. One is a restricted group of phages that specifically uses *B. fragilis* strain HSP40 as host. This group of phages appears unique, because it is found only in human faeces and not in faeces of other animals. The numbers of these phages in sewage appear to be relatively low, and they are almost absent in some geographical areas. The *B. fragilis* HSP40 phages belong to the family Siphoviridae, with flexible non-contractile tails, double-stranded DNA and capsids with a diameter of up to 60 nm. The second group of *Bacteroides* phages used as indicators is those that use *B. fragilis* strain RYC2056 as a host. This group includes a substantially wider spectrum of phages, occurring in the faeces of humans and many other animals. The numbers of these phages in sewage are generally substantially higher than those of *B. fragilis* HSP40 phages.

Indicator value

Bacteroides bacteriophages have been proposed as a possible index of faecal pollution due to their specific association with faecal material and exceptional resistance to environmental conditions. In particular, *B. fragilis* HSP40 phages are found only in human faeces. *Bacteroides fragilis* phage B40-8, a typical member of the group of *B. fragilis* HSP40 phages, has been found to be more resistant to inactivation by chlorine than poliovirus type 1, simian rotavirus SA11, coliphage f2, *E. coli* and *Streptococcus faecalis*. *Bacteroides fragilis* strain RYC2056 phages seem to be likewise relatively resistant

to disinfection. Indicator shortcomings of *B. fragilis* phages include relatively low numbers in sewage and polluted water environments. This applies in particular to *B. fragilis* HSP40 phages. Human enteric viruses have been detected in drinking-water supplies that yielded negative results in conventional tests for *B. fragilis* HSP40 phages. Owing to the limitations of *Bacteroides* bacteriophages, they are best used in laboratory investigations, pilot trials and possibly validation testing. They are not suitable for operational or verification (including surveillance) monitoring.

Source and occurrence

Bacteroides fragilis HSP40 phages are excreted by about 10–20% of humans in certain parts of the world; consequently, their numbers in sewage are substantially lower than those of somatic and even F-RNA coliphages. A mean count of 67 *B. fragilis* HSP40 phages per litre in a sewage-polluted river has been reported. In some parts of the world, *B. fragilis* HSP40 phages would appear not to be detectable in sewage at all. Phages using *B. fragilis* RYC2056 as host are excreted in larger numbers and seem to occur more universally. On average, these phages are excreted by more than 25% of humans. In a survey of water environments, *B. fragilis* HSP40 phages have been found to outnumber cytopathogenic enteric viruses on average by only about 5-fold. Theoretically, wastewaters could be expected to contain higher levels of *B. fragilis* phages than those detected. The reason for the discrepancy may be due to failure in maintaining sufficiently anaerobic conditions during the performance of plaque assays. Improvement of detection methods may result in the recording of higher numbers of *B. fragilis* phages in sewage and polluted water environments.

Application in practice

Disadvantages of *B. fragilis* phages are that the detection methods are more complex and expensive than those for coliphages. Costs are increased by the need to use antibiotics for purposes of selection and to incubate cultures and plaque assays under absolute anaerobic conditions. Results of plaque assays are usually available after about 24 h compared with about 8 h for coliphages.

Significance in drinking-water

The presence of *B. fragilis* phages in drinking-water is sound evidence of faecal pollution as well as shortcomings in water treatment and disinfection processes. In addition, the presence of *B. fragilis* HSP40 phages strongly indicates faecal pollution of human origin. However, *B. fragilis* phages occur in relatively low numbers in sewage, polluted water environments and drinking-water supplies. This implies that the absence of *B. fragilis* phages from treated drinking-water supplies does not confirm the absence of pathogens such as enteric viruses and protozoan parasites.

Selected bibliography

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Tartera C, Lucena F, Jofre J (1989) Human origin of *Bacteroides fragilis* bacteriophages present in the environment. *Applied and Environmental Microbiology*, 10:2696–2701.

11.6.8 Enteric viruses

General description

The viruses referred to here are a combined group of those that infect the human gastrointestinal tract and are predominantly transmitted by the faecal–oral route. Well known members of this group include the enteroviruses, astroviruses, enteric adenoviruses, orthoreoviruses, rotaviruses, caliciviruses and hepatitis A and E viruses. The enteric viruses cover a wide spectrum of viruses, members of which are a major cause of morbidity and mortality worldwide. Members of the group of enteric viruses differ with regard to structure, composition, nucleic acid and morphology. There are also differences in the numbers and frequency of excretion, survival in the environment and resistance to water treatment processes. Enteric viruses have robust capsids that enable them to survive unfavourable conditions in the environment as well as allowing passage through the acidic and proteolytic conditions in the stomach on their way to the duodenum, where they infect susceptible epithelial cells.

Indicator value

The use of enteric viruses as indicator or index organisms is based on the shortcomings of the existing choices. The survival of faecal bacteria in water environments and the sensitivity to treatment and disinfection processes differ substantially from those of enteric viruses. Monitoring based on one or more representatives of the large group of enteric viruses themselves would, therefore, be more valuable for assessment of the presence of any of the enteric viruses in water and the response to control measures.

Source and occurrence

Enteric viruses are excreted by individuals worldwide at a frequency and in numbers that result in many of these viruses being universally present in substantial numbers

in wastewater. However, the prevalence of individual members may vary to a large extent due to variations in rates of infection and excretion. Much higher numbers would be present during outbreaks.

Application in practice

Practical methods are not yet available for the routine monitoring of water supplies for a broad spectrum of enteric viruses. Viruses that are more readily detectable include members of the enterovirus, adenovirus and orthoreovirus groups. These viruses occur in polluted environments in relatively high numbers and can be detected by reasonably practical and moderate-cost techniques based on cytopathogenic effect in cell culture that yield results within 3–12 days (depending on the type of virus). In addition, progress in technology and expertise is decreasing costs. The cost for the recovery of enteric viruses from large volumes of drinking-water has been reduced extensively. Some techniques – for instance, those based on glass wool adsorption–elution – are inexpensive. The cost of cell culture procedures has also been reduced. Consequently, the cost of testing drinking-water supplies for cytopathogenic viruses has become acceptable for certain purposes. Testing could be used to validate effectiveness of treatment processes and, in certain circumstances, as part of specific investigations to verify performance of processes. The incubation times, cost and relative complexity of testing mean that enteric virus testing is not suitable for operational or verification (including surveillance) monitoring. Orthoreoviruses, and at least the vaccine strains of polioviruses detected in many water environments, also have the advantage of not constituting a health risk to laboratory workers.

Significance in drinking-water

The presence of any enteric viruses in drinking-water should be regarded as an index for the potential presence of other enteric viruses, is conclusive evidence of faecal pollution and also provides evidence of shortcomings in water treatment and disinfection processes.

Selected bibliography

Ashbolt NJ, Grabow WOK, Snozzi M (2001) Indicators of microbial water quality. In: Fewtrell L, Bartram J, eds. *Water quality: Guidelines, standards and health – Assessment of risk and risk management for water-related infectious disease*. WHO Water Series. London, IWA Publishing, pp. 289–315.

Grabow WOK, Taylor MB, de Villiers JC (2001) New methods for the detection of viruses: call for review of drinking-water quality guidelines. *Water Science and Technology*, 43:1–8.

12
Chemical fact sheets

The background documents referred to in this chapter may be found on the Water Sanitation and Health website at http://www.who.int/water_sanitation_health/dwq/guidelines/en/.

12.1 Acrylamide

Residual acrylamide monomer occurs in polyacrylamide coagulants used in the treatment of drinking-water. In general, the maximum authorized dose of polymer is 1 mg/litre. At a monomer content of 0.05%, this corresponds to a maximum theoretical concentration of 0.5 µg/litre of the monomer in water. Practical concentrations may be lower by a factor of 2–3. This applies to the anionic and non-ionic polyacrylamides, but residual levels from cationic polyacrylamides may be higher. Polyacrylamides are also used as grouting agents in the construction of drinking-water reservoirs and wells. Additional human exposure might result from food, owing to the use of polyacrylamide in food processing and the potential formation of acrylamide in foods cooked at high temperatures.

Guideline value	0.0005 mg/litre (0.5 µg/litre)
Occurrence	Concentrations of a few micrograms per litre have been detected in tap water.
Basis of guideline derivation	Combined mammary, thyroid and uterine tumours observed in female rats in a drinking-water study, and using the linearized multistage model
Limit of detection	0.032 µg/litre by GC; 0.2 µg/litre by HPLC; 10 µg/litre by HPLC with UV detection
Treatment achievability	Conventional treatment processes do not remove acrylamide. Acrylamide concentrations in drinking-water are controlled by limiting either the acrylamide content of polyacrylamide flocculants or the dose used, or both.
Additional comments	Although the practical quantification level for acrylamide in most laboratories is above the guideline value (generally in the order of 1 µg/litre), concentrations in drinking-water can be controlled by product and dose specification.

Toxicological review

Following ingestion, acrylamide is readily absorbed from the gastrointestinal tract and widely distributed in body fluids. Acrylamide can cross the placenta. It is neurotoxic, affects germ cells and impairs reproductive function. In mutagenicity assays, acrylamide was negative in the Ames test but induced gene mutations in mammalian cells and chromosomal aberrations *in vitro* and *in vivo*. In a long-term carcinogenicity study in rats exposed via drinking-water, acrylamide induced scrotal, thyroid and adrenal tumours in males and mammary, thyroid and uterine tumours in females. IARC has placed acrylamide in Group 2A. Recent data have shown that exposure to acrylamide from cooked food is much higher than previously thought. The significance of this new information for the risk assessment has not yet been determined.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to acrylamide. The 1993 Guidelines established a guideline value of 0.0005 mg/litre associated with an upper-bound excess lifetime cancer risk of 10^{-5}, noting that although the practical quantification level for acrylamide is generally in the order of 0.001 mg/litre, concentrations in drinking-water can be controlled by product and dose specification.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Acrylamide in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/71).

12.2 Alachlor

Alachlor (CAS No. 15972-60-8) is a pre- and post-emergence herbicide used to control annual grasses and many broad-leaved weeds in maize and a number of other crops. It is lost from soil mainly through volatilization, photodegradation and biodegradation. Many alachlor degradation products have been identified in soil.

Guideline value	0.02 mg/litre
Occurrence	Has been detected in groundwater and surface water; has also been detected in drinking-water at levels below 0.002 mg/litre
Basis of guideline derivation	Calculated by applying the linearized multistage model to data on the incidence of nasal tumours in rats
Limit of detection	0.1 µg/litre by gas–liquid chromatography with electrolytic conductivity detection in the nitrogen mode or by capillary column GC with a nitrogen–phosphorus detector
Treatment achievability	0.001 mg/litre should be achievable using GAC

Toxicological review

On the basis of available experimental data, evidence for the genotoxicity of alachlor is considered to be equivocal. However, a metabolite of alachlor, 2,6-diethylaniline, has been shown to be mutagenic. Available data from two studies in rats clearly indicate that alachlor is carcinogenic, causing benign and malignant tumours of the nasal turbinate, malignant stomach tumours and benign thyroid tumours.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to alachlor, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Alachlor was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines calculated a guideline value of 0.02 mg/litre for alachlor in drinking-water, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5}.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Alachlor in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/31).

12.3 Aldicarb

Aldicarb (CAS No. 116-06-3) is a systemic pesticide used to control nematodes in soil and insects and mites on a variety of crops. It is very soluble in water and highly mobile in soil. It degrades mainly by biodegradation and hydrolysis, persisting for weeks to months.

Guideline value	0.01 mg/litre
Occurrence	Frequently found as a contaminant in groundwater, particularly when associated with sandy soil; concentrations in well water as high as 500 µg/litre have been measured. Aldicarb sulfoxide and aldicarb sulfone residues are found in an approximately 1 : 1 ratio in groundwater.
ADI	0.003 mg/kg of body weight based on cholinesterase depression in a single oral dose study in human volunteers
Limit of detection	0.001 mg/litre by reverse-phase HPLC with fluorescence detection
Treatment achievability	0.001 mg/litre should be achievable using GAC or ozonation
Guideline derivation	
• allocation to water	10% of ADI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	The guideline value derived from the 1992 JMPR assessment was very similar to the guideline value derived in the second edition, which was therefore retained.

Toxicological review

Aldicarb is one of the most acutely toxic pesticides in use, although the only consistently observed toxic effect with both long-term and single-dose administration is acetylcholinesterase inhibition. It is metabolized to the sulfoxide and sulfone. Aldicarb sulfoxide is a more potent inhibitor of acetylcholinesterase than aldicarb itself, while aldicarb sulfone is considerably less toxic than either aldicarb or the sulfoxide. The weight of evidence indicates that aldicarb, aldicarb sulfoxide and aldicarb sulfone are not genotoxic or carcinogenic. IARC has concluded that aldicarb is not classifiable as to its carcinogenicity (Group 3).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to aldicarb, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Aldicarb was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but a health-based guideline value of 0.01 mg/litre was derived for aldicarb in the 1993 Guidelines.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1993) *Pesticide residues in food – 1992*. Rome, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Meeting on Pesticide Residues (Report No. 116).

WHO (2003) *Aldicarb in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/72).

12.4 Aldrin and dieldrin

Aldrin (CAS No. 309-00-2) and dieldrin (CAS No. 60-57-1) are chlorinated pesticides that are used against soil-dwelling pests, for wood protection and, in the case of dieldrin, against insects of public health importance. Since the early 1970s, a number of countries have either severely restricted or banned the use of both compounds, particularly in agriculture. The two compounds are closely related with respect to their toxicology and mode of action. Aldrin is rapidly converted to dieldrin under most environmental conditions and in the body. Dieldrin is a highly persistent organochlorine compound that has low mobility in soil, can be lost to the atmosphere and bioaccumulates. Dietary exposure to aldrin/dieldrin is very low and decreasing.

Guideline value	0.00003 mg/litre (0.03 µg/litre) combined aldrin and dieldrin
Occurrence	Concentrations of aldrin and dieldrin in drinking-water normally less than 0.01 µg/litre; rarely present in groundwater
PTDI	0.1 µg/kg of body weight (combined total for aldrin and dieldrin), based on NOAELs of 1 mg/kg of diet in the dog and 0.5 mg/kg of diet in the rat, which are equivalent to 0.025 mg/kg of body weight per day in both species, and applying an uncertainty factor of 250 based on concern about carcinogenicity observed in mice
Limit of detection	0.003 µg/litre for aldrin and 0.002 µg/litre for dieldrin by GC with ECD
Treatment achievability	0.02 µg/litre should be achievable using coagulation, GAC or ozonation
Guideline derivation • allocation to water • weight • consumption	 1% of PTDI 60-kg adult 2 litres/day
Additional comments	Aldrin and dieldrin are listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines.

Toxicological review

Both compounds are highly toxic in experimental animals, and cases of poisoning in humans have occurred. Aldrin and dieldrin have more than one mechanism of toxicity. The target organs are the central nervous system and the liver. In long-term studies, dieldrin was shown to produce liver tumours in both sexes of two strains of

mice. It did not produce an increase in tumours in rats and does not appear to be genotoxic. IARC has classified aldrin and dieldrin in Group 3. It is considered that all the available information on aldrin and dieldrin taken together, including studies on humans, supports the view that, for practical purposes, these chemicals make very little contribution, if any, to the incidence of cancer in humans.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to aldrin and dieldrin, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.03 µg/litre was recommended for aldrin and dieldrin, based on the ADI recommended by JMPR in 1970 for aldrin and dieldrin residues separately or together and reaffirmed by toxicological data available in 1977. The 1993 Guidelines confirmed the health-based guideline value of 0.03 µg/litre for aldrin and dieldrin, based on the reaffirmation of the ADI recommended in 1977 by JMPR.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1995) *Pesticide residues in food – 1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO Toxicological and Environmental Core Assessment Groups*. Rome, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 127).

WHO (2003) *Aldrin and dieldrin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/73).

12.5 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 for all sectors of the population. 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/toxicodynamic 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 1997 WHO EHC document for aluminium 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.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to aluminium. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 0.2 mg/litre was established for aluminium, based on aesthetic considerations (as a compromise between the use of aluminium compounds in water treatment and discoloration that may be observed if levels above 0.1 mg/litre remain in the distributed water). No health-based guideline value was recommended in the 1993 Guidelines, but the Guidelines confirmed that a concentration of 0.2 mg/litre in drinking-water provides a compromise between the practical use of aluminium salts in water treatment and discoloration of distributed water. No health-based guideline value was derived for aluminium in the addendum to the Guidelines published in 1998, owing to the limitations of the animal data as a model for humans and the uncertainty surrounding the human data. However, taking the beneficial effects of the use of aluminium as a coagulant in water treatment into account and considering the health concerns about aluminium (i.e., its potential neurotoxicity), a practicable level was derived based on optimization of the coagulation process in drinking-water plants using aluminium-based coagulants, to minimize aluminium levels in finished water. Under good operating conditions, concentrations of aluminium of 0.1 mg/litre or less are achievable in large water treatment facilities. For small facilities, 0.2 mg/litre or less is a practicable level for aluminium in finished water.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Aluminium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/53).

12.6 Ammonia

The term ammonia includes the non-ionized (NH_3) and ionized (NH_4^+) species. Ammonia in the environment originates from metabolic, agricultural and industrial processes and from disinfection with chloramine. Natural levels in groundwater and surface water are usually below 0.2 mg/litre. Anaerobic groundwaters may contain up to 3 mg/litre. Intensive rearing of farm animals can give rise to much higher levels in surface water. Ammonia contamination can also arise from cement mortar pipe

linings. Ammonia in water is an indicator of possible bacterial, sewage and animal waste pollution.

Ammonia is a major component of the metabolism of mammals. Exposure from environmental sources is insignificant in comparison with endogenous synthesis of ammonia. Toxicological effects are observed only at exposures above about 200 mg/kg of body weight.

Ammonia in drinking-water is not of immediate health relevance, and therefore no health-based guideline value is proposed. However, ammonia can compromise disinfection efficiency, result in nitrite formation in distribution systems, cause the failure of filters for the removal of manganese and cause taste and odour problems (see also chapter 10).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to ammonia. In the 1993 Guidelines, no health-based guideline value was recommended, but the Guidelines stated that ammonia could cause taste and odour problems at concentrations above 35 and 1.5 mg/litre, respectively.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Ammonia in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/1).

12.7 Antimony

Elemental antimony forms very hard alloys with copper, lead and tin. Antimony compounds have various therapeutic uses. Antimony was considered as a possible replacement for lead in solders, but there is no evidence of any significant contribution to drinking-water concentrations from this source. Daily oral uptake of antimony appears to be significantly higher than exposure by inhalation, although total exposure from environmental sources, food and drinking-water is very low compared with occupational exposure.

Guideline value	0.02 mg/litre
Occurrence	Concentrations in groundwater and surface water normally range from 0.1 to 0.2 µg/litre; concentrations in drinking-water appear to be less than 5 µg/litre.
TDI	6 µg/kg of body weight, based on a NOAEL of 6.0 mg/kg of body weight per day for decreased body weight gain and reduced food and water intake in a 90-day study in which rats were administered potassium antimony tartrate in drinking-water, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation, 10 for the short duration of the study)
Limit of detection	0.01 µg/litre by EAAS; 0.1–1 µg/litre by ICP/MS; 0.8 µg/litre by graphite furnace atomic absorption spectrophotometry; 5 µg/litre by hydride generation AAS
Treatment achievability	Conventional treatment processes do not remove antimony. However, antimony is not normally a raw water contaminant. As the most common source of antimony in drinking-water appears to be dissolution from metal plumbing and fittings, control of antimony from such sources would be by product control.
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

There has been a significant increase in the toxicity data available since the previous review, although much of it pertains to the intraperitoneal route of exposure. The form of antimony in drinking-water is a key determinant of the toxicity, and it would appear that antimony leached from antimony-containing materials would be in the form of the antimony(V) oxo-anion, which is the less toxic form. The subchronic toxicity of antimony trioxide is lower than that of potassium antimony tartrate, which is the most soluble form. Antimony trioxide, due to its low bioavailability, is genotoxic only in some *in vitro* tests, but not *in vivo*, whereas soluble antimony(III) salts exert genotoxic effects *in vitro* and *in vivo.* Animal experiments from which the carcinogenic potential of soluble or insoluble antimony compounds may be quantified are not available. IARC has concluded that antimony trioxide is possibly carcinogenic to humans (Group 2B) on the basis of an inhalation study in rats, but that antimony trisulfide was not classifiable as to its carcinogenicity to humans (Group 3). However, chronic oral uptake of potassium antimony tartrate may not be associated with an additional carcinogenic risk, since antimony after inhalation exposure was carcinogenic only in the lung but not in other organs and is known to cause direct lung damage following chronic inhalation as a consequence of overload with insoluble particulates. Although there is some evidence for the carcinogenicity of certain antimony compounds by inhalation, there are no data to indicate carcinogenicity by the oral route.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to antimony. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that no action was required for antimony. A provisional guideline value for antimony was set at a practical quantification level of 0.005 mg/litre in the 1993 Guidelines, based on available toxicological data.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Antimony in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/74).

12.8 Arsenic

Arsenic is widely distributed throughout the Earth's crust, most often as arsenic sulfide or as metal arsenates and arsenides. Arsenicals are used commercially and industrially, primarily as alloying agents in the manufacture of transistors, lasers and semiconductors. Arsenic is introduced into drinking-water sources primarily through the dissolution of naturally occurring minerals and ores. Except for individuals who are occupationally exposed to arsenic, the most important route of exposure is through the oral intake of food and beverages. There are a number of regions where arsenic may be present in drinking-water sources, particularly groundwater, at elevated concentrations. Arsenic in drinking-water is a significant cause of health effects in some areas, and arsenic is considered to be a high-priority substance for screening in drinking-water sources. Concentrations are often highly dependent on the depth to which the well is sunk.

Provisional guideline value	0.01 mg/litre The guideline value is designated as provisional in view of the scientific uncertainties.
Occurrence	Levels in natural waters generally range between 1 and 2 µg/litre, although concentrations may be elevated (up to 12 mg/litre) in areas containing natural sources.
Basis of guideline derivation	There remains considerable uncertainty over the actual risks at low concentrations, and available data on mode of action do not provide a biological basis for using either linear or non-linear extrapolation. In view of the significant uncertainties surrounding the risk assessment for arsenic carcinogenicity, the practical quantification limit in the region of 1–10 µg/litre and the practical difficulties in removing arsenic from drinking-water, the guideline value of 10 µg/litre is retained. In view of the scientific uncertainties, the guideline value is designated as provisional.

Limit of detection	0.1 µg/litre by ICP/MS; 2 µg/litre by hydride generation AAS or FAAS
Treatment achievability	It is technically feasible to achieve arsenic concentrations of 5 µg/litre or lower using any of several possible treatment methods. However, this requires careful process optimization and control, and a more reasonable expectation is that 10 µg/litre should be achievable by conventional treatment, e.g., coagulation.
Additional comments	• A management guidance document on arsenic is available. • In many countries, this guideline value may not be attainable. Where this is the case, every effort should be made to keep concentrations as low as possible.

Toxicological review

Arsenic has not been demonstrated to be essential in humans. It is an important drinking-water contaminant, as it is one of the few substances shown to cause cancer in humans through consumption of drinking-water. There is overwhelming evidence from epidemiological studies that consumption of elevated levels of arsenic through drinking-water is causally related to the development of cancer at several sites, particularly skin, bladder and lung. In several parts of the world, arsenic-induced disease, including cancer, is a significant public health problem. Because trivalent inorganic arsenic has greater reactivity and toxicity than pentavalent inorganic arsenic, it is generally believed that the trivalent form is the carcinogen. However, there remain considerable uncertainty and controversy over both the mechanism of carcinogenicity and the shape of the dose–response curve at low intakes. Inorganic arsenic compounds are classified by IARC in Group 1 (carcinogenic to humans) on the basis of sufficient evidence for carcinogenicity in humans and limited evidence for carcinogenicity in animals.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.2 mg/litre for arsenic, based on health concerns. In the 1963 International Standards, this value was lowered to 0.05 mg/litre, which was retained as a tentative upper concentration limit in the 1971 International Standards. The guideline value of 0.05 mg/litre was also retained in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984. A provisional guideline value for arsenic was set at the practical quantification limit of 0.01 mg/litre in the 1993 Guidelines, based on concern regarding its carcinogenicity in humans.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2001) *Arsenic and arsenic compounds*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 224).

WHO (2003) *Arsenic in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/75).

12.9 Asbestos

Asbestos is introduced into water by the dissolution of asbestos-containing minerals and ores as well as from industrial effluents, atmospheric pollution and asbestos-cement pipes in the distribution system. Exfoliation of asbestos fibres from asbestos-cement pipes is related to the aggressiveness of the water supply. Limited data indicate that exposure to airborne asbestos released from tap water during showers or humidification is negligible.

Asbestos is a known human carcinogen by the inhalation route. Although well studied, there has been little convincing evidence of the carcinogenicity of ingested asbestos in epidemiological studies of populations with drinking-water supplies containing high concentrations of asbestos. Moreover, in extensive studies in animal species, asbestos has not consistently increased the incidence of tumours of the gastrointestinal tract. There is, therefore, no consistent evidence that ingested asbestos is hazardous to health, and thus it is concluded that there is no need to establish a health-based guideline value for asbestos in drinking-water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to asbestos. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was noted that available data were insufficient to determine whether a guideline value was needed for asbestos. The 1993 Guidelines concluded that there was no consistent evidence that ingested asbestos was hazardous to health and that there was therefore no need to establish a health-based guideline value for asbestos in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Asbestos in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/2).

12.10 Atrazine

Atrazine (CAS No. 1912-24-9) is a selective pre- and early post-emergence herbicide. It has been found in surface water and groundwater as a result of its mobility in soil.

It is relatively stable in soil and aquatic environments, with a half-life measured in months, but is degraded by photolysis and microbial action in soil.

Guideline value	0.002 mg/litre
Occurrence	Found in groundwater and drinking-water at levels below 10 µg/litre
TDI	0.5 µg/kg of body weight based on a NOAEL of 0.5 mg/kg of body weight per day in a carcinogenicity study in the rat and an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 to reflect potential neoplasia)
Limit of detection	0.01 µg/litre by GC/MS
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

The weight of evidence from a wide variety of genotoxicity assays indicates that atrazine is not genotoxic. There is evidence that atrazine can induce mammary tumours in rats. It is highly probable that the mechanism for this process is non-genotoxic. No significant increase in neoplasia has been observed in mice. IARC has concluded that atrazine is not classifiable as to its carcinogenicity in humans (Group 3).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to atrazine, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Atrazine was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.002 mg/litre for atrazine in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Atrazine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/32).

12.11 Barium

Barium is present as a trace element in both igneous and sedimentary rocks, and barium compounds are used in a variety of industrial applications; however, barium in water comes primarily from natural sources. Food is the primary source of intake for the non-occupationally exposed population. However, where barium levels in water are high, drinking-water may contribute significantly to total intake.

Guideline value	0.7 mg/litre
Occurrence	Concentrations in drinking-water are generally below 100 µg/litre, although concentrations above 1 mg/litre have been measured in drinking-water derived from groundwater.
NOAEL in humans	7.3 mg/litre in the most sensitive epidemiological study conducted to date, in which there were no significant differences in blood pressure or in the prevalence of cardiovascular disease between a population drinking water containing a mean barium concentration of 7.3 mg/litre and one whose water contained a barium concentration of 0.1 mg/litre
Guideline derivation	Uncertainty factor of 10 for intraspecies variation applied to NOAEL in humans
Limit of detection	0.1 µg/litre by ICP/MS; 2 µg/litre by AAS; 3 µg/litre by ICP/optical emission spectroscopy
Treatment achievability	0.1 mg/litre should be achievable using either ion exchange or precipitation softening; other conventional processes are ineffective
Additional comments	The guideline value for barium is based on an epidemiological study in which no adverse effects were observed, although the study population was relatively small and the power of the study was limited. As a consequence, an uncertainty factor of 10 was applied to the level of barium in the drinking-water of the study population. However, the level at which effects would be seen may be significantly greater than this concentration, so the guideline value for barium may be highly conservative and the margin of safety is likely to be high.

Toxicological review

There is no evidence that barium is carcinogenic or mutagenic. Barium has been shown to cause nephropathy in laboratory animals, but the toxicological end-point of greatest concern to humans appears to be its potential to cause hypertension.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* did not refer to barium. The 1963 International Standards recommended a maximum allowable concentration of 1.0 mg/litre, based on health concerns. The 1971 International Standards stated that barium should be controlled in drinking-water, but that insufficient information was available to enable a tentative limit to be established. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that it was

not necessary to establish a guideline value for barium in drinking-water, as there was no firm evidence of any health effects associated with the normally low levels of barium in water. A health-based guideline value of 0.7 mg/litre was derived for barium in the 1993 Guidelines, based on concern regarding the potential of barium to cause hypertension.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2001) *Barium and barium compounds*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 33).

WHO (2003) *Barium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/76).

12.12 Bentazone

Bentazone (CAS No. 25057-89-0) is a broad-spectrum herbicide used for a variety of crops. Photodegradation occurs in soil and water; however, bentazone is very mobile in soil and moderately persistent in the environment. Bentazone has been reported to occur in surface water, groundwater and drinking-water at concentrations of a few micrograms per litre or less. Although it has been found in groundwater and has a high affinity for the water compartment, it does not seem to accumulate in the environment. Exposure from food is unlikely to be high.

Long-term studies conducted in rats and mice have not indicated a carcinogenic potential, and a variety of *in vitro* and *in vivo* assays have indicated that bentazone is not genotoxic. A health-based value of 300 µg/litre can be calculated on the basis of an ADI of 0.1 mg/kg of body weight established by JMPR, based on haematological effects observed in a 2-year dietary study in rats. However, because bentazone occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to bentazone, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Bentazone was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.03 mg/litre for bentazone, based on an ADI established by JMPR in 1991. This guideline value was amended to 0.3 mg/litre in the addendum to the Guidelines, published in 1998, based on new information on the environmental behaviour of bentazone and exposure from food.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1999) *Pesticide residues in food – 1998. Evaluations – 1998. Part II – Toxicology.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/01.12).

WHO (2003) *Bentazone in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/77).

12.13 Benzene

Benzene is used principally in the production of other organic chemicals. It is present in petrol, and vehicular emissions constitute the main source of benzene in the environment. Benzene may be introduced into water by industrial effluents and atmospheric pollution.

Guideline value	0.01 mg/litre
Occurrence	Concentrations in drinking-water generally less than 5 µg/litre
Basis of guideline derivation	Robust linear extrapolation model (because of statistical lack of fit of some of the data with the linearized multistage model) applied to leukaemia and lymphomas in female mice and oral cavity squamous cell carcinomas in male rats in a 2-year gavage study in rats and mice
Limit of detection	0.2 µg/litre by GC with photoionization detection and confirmation by MS
Treatment achievability	0.01 mg/litre should be achievable using GAC or air stripping
Additional comments	Lower end of estimated range of concentrations in drinking-water corresponding to an upper-bound excess lifetime cancer risk of 10^{-5} (10–80 µg/litre) corresponds to the estimate derived from data on leukaemia from epidemiological studies involving inhalation exposure, which formed the basis for the previous guideline value. The previous guideline value is therefore retained.

Toxicological review

Acute exposure of humans to high concentrations of benzene primarily affects the central nervous system. At lower concentrations, benzene is toxic to the haematopoietic system, causing a continuum of haematological changes, including leukaemia. Because benzene is carcinogenic to humans, IARC has classified it in Group 1. Haematological abnormalities similar to those observed in humans have been observed in animal species exposed to benzene. In animal studies, benzene was shown to be carcinogenic following both inhalation and ingestion. It induced several types of tumours in both rats and mice in a 2-year carcinogenesis bioassay by gavage in corn oil. Benzene has not been found to be mutagenic in bacterial assays, but it has been shown to cause chromosomal aberrations *in vivo* in a number of species, including humans, and to be positive in the mouse micronucleus test.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to benzene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.01 mg/litre was recommended for

benzene based on human leukaemia data from inhalation exposure applied to a linear multistage extrapolation model. The 1993 Guidelines estimated the range of benzene concentrations in drinking-water corresponding to an upper-bound excess lifetime cancer risk of 10^{-5} to be 0.01–0.08 mg/litre based on carcinogenicity in female mice and male rats. As the lower end of this estimate corresponds to the estimate derived from epidemiological data, which formed the basis for the previous guideline value of 0.01 mg/litre associated with a 10^{-5} upper-bound excess lifetime cancer risk, the guideline value of 0.01 mg/litre was retained.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Benzene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/24).

12.14 Boron

Boron compounds are used in the manufacture of glass, soaps and detergents and as flame retardants. The general population obtains the greatest amount of boron through food intake, as it is naturally found in many edible plants. Boron is found naturally in groundwater, but its presence in surface water is frequently a consequence of the discharge of treated sewage effluent, in which it arises from use in some detergents, to surface waters.

Provisional guideline value	0.5 mg/litre The guideline is designated as provisional because it will be difficult to achieve in areas with high natural boron levels with the treatment technology available.
Occurrence	Concentrations vary widely and depend on the surrounding geology and wastewater discharges. For most of the world, the concentration range of boron in drinking-water is judged to be between 0.1 and 0.3 mg/litre.
TDI	0.16 mg/kg of body weight, based on a NOAEL of 9.6 mg/kg of body weight per day for developmental toxicity (decreased fetal body weight in rats) and an uncertainty factor of 60 (10 for interspecies variation and 6 for intraspecies variation)
Limit of detection	0.2 µg/litre by ICP/MS; 6–10 µg/litre by ICP/AES

Treatment achievability	Conventional water treatment (coagulation, sedimentation, filtration) does not significantly remove boron, and special methods need to be installed in order to remove boron from waters with high boron concentrations. Ion exchange and reverse osmosis processes may enable substantial reduction but are likely to be prohibitively expensive. Blending with low-boron supplies may be the only economical method to reduce boron concentrations in waters where these concentrations are high.
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

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. 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.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to boron. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that no action was required for boron. A health-based guideline value of 0.3 mg/litre for boron was established in the 1993 Guidelines, while noting that boron's removal by drinking-water treatment appears to be poor. This guideline value was increased to 0.5 mg/litre in the addendum to the Guidelines published in 1998 and was designated as provisional because, with the treatment technology available, the guideline value will be difficult to achieve in areas with high natural boron levels.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Boron in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/54).

12.15 Bromate

Sodium and potassium bromate are powerful oxidizers used mainly in permanent wave neutralizing solutions and the dyeing of textiles using sulfur dyes. Potassium bromate is also used as an oxidizer to mature flour during milling, in treating barley in beer making and in fish paste products, although JECFA has concluded that the use of potassium bromate in food processing is not appropriate. Bromate is not normally found in water, but may be formed during ozonation when the bromide ion is present in water. Under certain conditions, bromate may also be formed in concentrated hypochlorite solutions used to disinfect drinking-water.

Provisional guideline value	0.01 mg/litre The guideline value is provisional because of limitations in available analytical and treatment methods.
Occurrence	Has been reported in drinking-water with a variety of source water characteristics after ozonation at concentrations ranging from <2 to 293 µg/litre, depending on bromide ion concentration, ozone dosage, pH, alkalinity and dissolved organic carbon; can also be formed in the electrolytic generation of chlorine and hypochlorite from brine with a high level of bromide contamination
Basis of guideline derivation	Upper-bound estimate of cancer potency for bromate is 0.19 per mg/kg of body weight per day, based on low-dose linear extrapolation (a one-stage Weibull time-to-tumour model was applied to the incidence of mesotheliomas, renal tubule tumours and thyroid follicular tumours in male rats given potassium bromate in drinking-water, using the 12-, 26-, 52- and 77-week interim kill data). A health-based value of 2 µg/litre is associated with the upper-bound excess cancer risk of 10^{-5}. A similar conclusion may be reached through several other methods of extrapolation, leading to values in the range 2–6 µg/litre.
Limit of detection	1.5 µg/litre by ion chromatography with suppressed conductivity detection; 0.2 µg/litre by ion chromatography with UV/visible absorbance detection; 0.3 µg/litre by ion chromatography with detection by ICP/MS
Treatment achievability	Bromate is difficult to remove once formed. By appropriate control of disinfection conditions, it is possible to achieve bromate concentrations below 0.01 mg/litre.

Toxicological review

IARC has concluded that although there is inadequate evidence of carcinogenicity in humans, there is sufficient evidence for the carcinogenicity of potassium bromate in experimental animals and has classified it in Group 2B (possibly carcinogenic to humans). Bromate is mutagenic both *in vitro* and *in vivo*. At this time, there is not sufficient evidence to conclude the mode of carcinogenic action for potassium bromate. Observation of tumours at a relatively early time and the positive response of bromate in a variety of genotoxicity assays suggest that the predominant mode of action at low doses is due to DNA reactivity. Although there is limited evidence to

suggest that the DNA reactivity in kidney tumours may have a non-linear dose–response relationship, there is no evidence to suggest that this same dose–response relationship operates in the development of mesotheliomas or thyroid tumours. Oxidative stress may play a role in the formation of kidney tumours, but the evidence is insufficient to establish lipid peroxidation and free radical production as key events responsible for induction of kidney tumours. Also, there are no data currently available to suggest that any single mechanism, including oxidative stress, is responsible for the production of thyroid and peritoneal tumours by bromate.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to bromate. The 1993 Guidelines calculated the concentration of bromate in drinking-water associated with an upper-bound excess lifetime cancer risk of 10^{-5} to be 0.003 mg/litre. However, because of limitations in available analytical and treatment methods, a provisional guideline value of 0.025 mg/litre, associated with an upper-bound excess lifetime cancer risk of 7×10^{-5}, was recommended.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Bromate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/78).

12.16 Brominated acetic acids

Brominated acetic acids are formed during disinfection of water that contains bromide ions and organic matter. Bromide ions occur naturally in surface water and groundwater and exhibit seasonal fluctuations in levels. Bromide ion levels can increase due to saltwater intrusion resulting from drought conditions or due to pollution. Brominated acetates are generally present in surface water and groundwater distribution systems at mean concentrations below 5 µg/litre.

The database for dibromoacetic acid is considered inadequate for the derivation of a guideline value. There are no systemic toxicity studies of subchronic duration or longer. The database also lacks suitable toxicokinetic studies, a carcinogenicity study, a developmental study in a second species and a multigeneration reproductive toxicity study (one has been conducted but is currently being evaluated by the US EPA). Available mutagenicity data suggest that dibromoacetate is genotoxic.

Data are also limited on the oral toxicity of monobromoacetic acid and bromochloroacetic acid. Limited mutagenicity and genotoxicity data give mixed results for monobromoacetic acid and generally positive results for bromochloroacetic acid.

Data gaps include subchronic or chronic toxicity studies, multigeneration reproductive toxicity studies, standard developmental toxicity studies and carcinogenicity studies. The available data are considered inadequate to establish guideline values for these chemicals.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to brominated acetic acids. Brominated acetic acids were not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2000) *Disinfectants and disinfectant by-products*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2003) *Brominated acetic acids in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/79).

12.17 Cadmium

Cadmium metal is used in the steel industry and in plastics. Cadmium compounds are widely used in batteries. Cadmium is released to the environment in wastewater, and diffuse pollution is caused by contamination from fertilizers and local air pollution. Contamination in drinking-water may also be caused by impurities in the zinc of galvanized pipes and solders and some metal fittings. Food is the main source of daily exposure to cadmium. The daily oral intake is 10–35 µg. Smoking is a significant additional source of cadmium exposure.

Guideline value	0.003 mg/litre
Occurrence	Levels in drinking-water usually less than 1 µg/litre
PTWI	7 µg/kg of body weight, on the basis that if levels of cadmium in the renal cortex are not to exceed 50 mg/kg, total intake of cadmium (assuming an absorption rate for dietary cadmium of 5% and a daily excretion rate of 0.005% of body burden) should not exceed 1 µg/kg of body weight per day
Limit of detection	0.01 µg/litre by ICP/MS; 2 µg/litre by FAAS
Treatment achievability	0.002 mg/litre should be achievable using coagulation or precipitation softening

Guideline derivation	
• allocation to water	10% of PTWI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	• Although new information indicates that a proportion of the general population may be at increased risk for tubular dysfunction when exposed at the current PTWI, the risk estimates that can be made at present are imprecise. • It is recognized that the margin between the PTWI and the actual weekly intake of cadmium by the general population is small, less than 10-fold, and that this margin may be even smaller in smokers.

Toxicological review

Absorption of cadmium compounds is dependent on the solubility of the compounds. Cadmium accumulates primarily in the kidneys and has a long biological half-life in humans of 10–35 years. There is evidence that cadmium is carcinogenic by the inhalation route, and IARC has classified cadmium and cadmium compounds in Group 2A. However, there is no evidence of carcinogenicity by the oral route and no clear evidence for the genotoxicity of cadmium. The kidney is the main target organ for cadmium toxicity. The critical cadmium concentration in the renal cortex that would produce a 10% prevalence of low-molecular-weight proteinuria in the general population is about 200 mg/kg and would be reached after a daily dietary intake of about 175 µg per person for 50 years.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* did not refer to cadmium. The 1963 International Standards recommended a maximum allowable concentration of 0.01 mg/litre, based on health concerns. This value was retained in the 1971 International Standards as a tentative upper concentration limit, based on the lowest concentration that could be conveniently measured. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 0.005 mg/litre was recommended for cadmium in drinking-water. This value was lowered to 0.003 mg/litre in the 1993 Guidelines, based on the PTWI set by JECFA.

Assessment date

The risk assessment was conducted in 2003.

Principal references

JECFA (2000) *Summary and conclusions of the fifty-fifth meeting, Geneva, 6–15 June 2000*. Geneva, World Health Organization, Joint FAO/WHO Expert Committee on Food Additives.

WHO (2003) *Cadmium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/80).

12.18 Carbofuran

Carbofuran (CAS No. 1563-66-2) is used worldwide as a pesticide 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.

Guideline value	0.007 mg/litre
Occurrence	Has been detected in surface water, groundwater and drinking-water, generally at levels of a few micrograms per litre or lower; highest concentration (30 µg/litre) measured in groundwater
ADI	0.002 mg/kg of body weight based on a NOAEL of 0.22 mg/kg of body weight per day for acute (reversible) effects in dogs in a short-term (4-week) study conducted as an adjunct to a 13-week study in which inhibition of erythrocyte acetylcholinesterase activity was observed, and using an uncertainty factor of 100
Limit of detection	0.1 µg/litre by GC with a nitrogen–phosphorus detector; 0.9 µg/litre by reverse-phase HPLC with a fluorescence detector
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 10% of ADI 60-kg adult 2 litres/day
Additional comments	Use of a 4-week study was considered appropriate because the NOAEL is based on a reversible acute effect; the NOAEL will also be protective for chronic effects.

Toxicological review

Carbofuran is highly toxic after acute oral administration. The main systemic effect of carbofuran poisoning in short- and long-term toxicity studies appears to be cholinesterase inhibition. No evidence of teratogenicity has been found in reproductive toxicity studies. On the basis of available studies, carbofuran does not appear to be carcinogenic or genotoxic.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to carbofuran, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Carbofuran was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but a

health-based guideline value of 0.005 mg/litre was established for carbofuran in the 1993 Guidelines, based on human data and supported by observations in laboratory animals. This value was amended to 0.007 mg/litre in the addendum to the Guidelines published in 1998, on the basis of the ADI established by JMPR in 1996.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal references

FAO/WHO (1997) *Pesticide residues in food – 1996. Evaluations – 1996. Part II – Toxicological.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/97.1).

WHO (2003) *Carbofuran in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/81).

12.19 Carbon tetrachloride

Carbon tetrachloride is used mainly in the production of chlorofluorocarbon refrigerants, foam-blowing agents and solvents. 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 and use have dropped and will continue to drop. Carbon tetrachloride is released mostly into the atmosphere but also into industrial wastewater. Although it readily migrates from surface water to the atmosphere, levels in anaerobic groundwater may remain elevated for months or even years. 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.

Guideline value	0.004 mg/litre
Occurrence	Concentrations in drinking-water generally less than 5 µg/litre
TDI	1.4 µg/kg of body weight, based on a NOAEL of 1 mg/kg of body weight per day for hepatotoxic effects in a 12-week oral gavage study in rats, 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)
Limit of detection	0.1–0.3 µg/litre by GC with ECD or MS
Treatment achievability	0.001 mg/litre should be achievable using air stripping

Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	The guideline value is lower than the range of values associated with upper-bound lifetime excess cancer risks of 10^{-4}, 10^{-5} and 10^{-6} calculated by linear extrapolation.

Toxicological review

The primary targets for carbon tetrachloride toxicity are liver and kidney. 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. On the basis of available data, carbon tetrachloride can be considered to be a non-genotoxic compound. Carbon tetrachloride is classified by IARC 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.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to carbon tetrachloride. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a tentative guideline value of 0.003 mg/litre was recommended; the guideline was designated as tentative because reliable evidence on which to calculate a guideline value based on carcinogenicity was available in only one animal species, because of the good qualitative supporting data and because of its frequency of occurrence in water. The 1993 Guidelines established a health-based guideline value of 0.002 mg/litre for carbon tetrachloride.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1999) *Carbon tetrachloride*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 208).

WHO (2003) *Carbon tetrachloride in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/82).

12.20 Chloral hydrate (trichloroacetaldehyde)

Chloral hydrate can be formed as a by-product of the chlorination of water containing organic precursor material, such as fulvic and humic acids. It has been found in drinking-water at concentrations of up to 100 µg/litre, but concentrations are usually

below 10 µg/litre. Concentrations are generally higher in surface water than in groundwater, and concentrations appear to increase during distribution.

Chloral hydrate is used as an intermediate in the production of insecticides, herbicides and hypnotic drugs. It has also been widely used as a sedative or hypnotic drug in humans at oral doses of up to about 750–1000 mg/day. Although intake from clinical use is considerably higher than intake from drinking-water, clinical exposure is of shorter-term duration.

No epidemiological or carcinogenic studies were found in humans that associated exposure to chloral hydrate with cancer, despite the fact that chloral hydrate has been used for many decades (and still is used) as a sedative and hypnotic drug in adults and children (specifically for dental procedures). IARC classified chloral hydrate as not classifiable as to its carcinogenicity to humans (Group 3), based on inadequate evidence in humans and limited evidence in experimental animals. There is equivocal evidence of genotoxicity for chloral hydrate.

A health-based value of 0.1 mg/litre (rounded figure) can be calculated on the basis of a TDI of 0.0045 mg/kg of body weight per day derived based on an increased incidence of liver histopathology observed in B6C3F1 mice in a 2-year drinking-water study, allocating 80% of the TDI to drinking-water (because most exposure to chloral hydrate is from drinking-water) and assuming a 60-kg adult consuming 2 litres of water per day. However, because chloral hydrate usually occurs in drinking-water at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

Chloral hydrate levels in drinking-water can be controlled by changes to disinfection practice (e.g., enhanced coagulation and softening to remove organic precursor compounds, moving the point of disinfection to reduce the reaction between chlorine and precursor compounds and using chloramines for residual disinfection instead of chlorine) and by GAC treatment.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chloral hydrate. The 1993 Guidelines established a provisional health-based guideline value of 0.01 mg/litre for chloral hydrate in drinking-water. The guideline value was designated as provisional because of the limitations of the available database, necessitating the use of an uncertainty factor of 10 000. This guideline value was brought forward to the third edition of the Guidelines.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (2000) *Chloral hydrate*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 25).

IPCS (2000) *Disinfectants and disinfectant by-products*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2005) *Chloral hydrate in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/49).

12.21 Chlordane

Chlordane (CAS No. 57-47-9) is a broad-spectrum insecticide that has been used since 1947. Its use has recently been increasingly restricted in many countries, and it is now used mainly to destroy termites by subsurface injection into soil. Chlordane may be a low-level source of contamination of groundwater when applied by subsurface injection. Technical chlordane is a mixture of compounds, with the *cis* and *trans* forms of chlordane predominating. It is very resistant to degradation, is highly immobile in soil and it unlikely to migrate to groundwater, where it has only rarely been found. It is readily lost to the atmosphere. Although levels of chlordane in food have been decreasing, it is highly persistent and has a high bioaccumulation potential.

Guideline value	0.0002 mg/litre (0.2 µg/litre)
Occurrence	Has been detected in both drinking-water and groundwater, usually at levels below 0.1 µg/litre
PTDI	0.5 µg/kg of body weight based on a NOAEL of 50 µg/kg of body weight per day for increased liver weights, serum bilirubin levels and incidence of hepatocellular swelling, derived from a long-term dietary study in rats, and using an uncertainty factor of 100
Limit of detection	0.014 µg/litre by GC with an ECD
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 1% of PTDI 60-kg adult 2 litres/day
Additional comments	Chlordane is listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines.

Toxicological review

In experimental animals, prolonged exposure in the diet causes liver damage. Chlordane produces liver tumours in mice, but the weight of evidence indicates that it is not genotoxic. Chlordane can interfere with cell communication *in vitro*, a characteristic of many tumour promoters. IARC re-evaluated chlordane in 1991 and concluded that there is inadequate evidence for its carcinogenicity in humans and sufficient evidence for its carcinogenicity in animals, classifying it in Group 2B.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlordane, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.3 µg/litre was recommended for chlordane (total isomers), based on the

ADI recommended by JMPR in 1977. The 1993 Guidelines established a health-based guideline value of 0.2 µg/litre for chlordane in drinking-water, based on an ADI established by JMPR in 1986.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1995) *Pesticide residues in food – 1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO Toxicological and Environmental Core Assessment Groups*. Rome, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 127).

WHO (2003) *Chlordane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/84).

12.22 Chloride

Chloride in drinking-water originates from natural sources, sewage and industrial effluents, urban runoff containing de-icing salt and saline intrusion.

The main source of human exposure to chloride is the addition of salt to food, and the intake from this source is usually greatly in excess of that from drinking-water.

Excessive chloride concentrations increase rates of corrosion of metals in the distribution system, depending on the alkalinity of the water. This can lead to increased concentrations of metals in the supply.

No health-based guideline value is proposed for chloride in drinking-water. However, chloride concentrations in excess of about 250 mg/litre can give rise to detectable taste in water (see chapter 10).

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of chloride greater than 600 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 250 mg/litre was established for chloride, based on taste considerations. No health-based guideline value for chloride in drinking-water was proposed in the 1993 Guidelines, although it was confirmed that chloride concentrations in excess of about 250 mg/litre can give rise to detectable taste in water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chloride in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/3).

12.23 Chlorine

Chlorine is produced in large amounts and widely used both industrially and domestically as an important disinfectant and bleach. In particular, it is widely used in the disinfection of swimming pools and is the most commonly used disinfectant and oxidant in drinking-water treatment. In water, chlorine reacts to form hypochlorous acid and hypochlorites.

Guideline value	5 mg/litre
Occurrence	Present in most disinfected drinking-water at concentrations of 0.2–1 mg/litre
TDI	150 µg/kg of body weight, derived from a NOAEL for the absence of toxicity in rodents ingesting chlorine in drinking-water for 2 years
Limit of detection	0.01 µg/litre following pre-column derivatization to 4-bromoacetanilide by HPLC; 10 µg/litre as free chlorine by colorimetry; 0.2 mg/litre by ion chromatography
Treatment achievability	It is possible to reduce the concentration of chlorine effectively to zero (< 0.1 mg/litre) by reduction. However, it is normal practice to supply water with a chlorine residual of a few tenths of a milligram per litre to act as a preservative during distribution.
Guideline derivation	
• allocation to water	100% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	• The guideline value is conservative, as no adverse effect level was identified in the critical study. • Most individuals are able to taste chlorine at the guideline value.

Toxicological review

In humans and animals exposed to chlorine in drinking-water, no specific adverse treatment-related effects have been observed. IARC has classified hypochlorite in Group 3.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chlorine. The 1993 Guidelines established a guideline value of 5 mg/litre for free chlorine in drinking-water, but noted that this value is conservative, as no adverse effect level was identified in the study used. It was also noted that most individuals are able to taste chlorine at the guideline value.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/45).

12.24 Chlorite and chlorate

Chlorite and chlorate are DBPs resulting from the use of chlorine dioxide as a disinfectant and for odour/taste control in water. Chlorine dioxide is also used as a bleaching agent for cellulose, paper pulp, flour and oils. Sodium chlorite and sodium chlorate are both used in the production of chlorine dioxide as well as for other commercial purposes. Chlorine dioxide rapidly decomposes into chlorite, chlorate and chloride ions in treated water, chlorite being the predominant species; this reaction is favoured by alkaline conditions. The major route of environmental exposure to chlorine dioxide, sodium chlorite and sodium chlorate is through drinking-water.

Provisional guideline values	
Chlorite	0.7 mg/litre
Chlorate	0.7 mg/litre The guideline values for chlorite and chlorate are designated as provisional because use of chlorine dioxide as a disinfectant may result in the chlorite and chlorate guideline values being exceeded, and difficulties in meeting the guideline value must never be a reason for compromising adequate disinfection.
Occurrence	Levels of chlorite in water reported in one study ranged from 3.2 to 7.0 mg/litre; however, the combined levels will not exceed the dose of chlorine dioxide applied. Chlorate can also form in hypochlorite solutions on storage.

TDIs	
Chlorite	30 µg/kg of body weight based on a NOAEL of 2.9 mg/kg of body weight per day identified in a two-generation study in rats, based on lower startle amplitude, decreased absolute brain weight in the F_1 and F_2 generations and altered liver weights in two generations, using an uncertainty factor of 100 (10 each for inter- and intraspecies variation)
Chlorate	30 µg/kg of body weight based on a NOAEL of 30 mg/kg of body weight per day in a recent well conducted 90-day study in rats, based on thyroid gland colloid depletion at the next higher dose, and using an uncertainty factor of 1000 (10 each for inter- and intraspecies variation and 10 for the short duration of the study)
Limit of detection	5 µg/litre by ion chromatography with suppressed conductivity detection for chlorate
Treatment achievability	It is possible to reduce the concentration of chlorine dioxide effectively to zero (< 0.1 mg/litre) by reduction; however, it is normal practice to supply water with a chlorine dioxide residual of a few tenths of a milligram per litre to act as a preservative during distribution. Chlorate concentrations arising from the use of sodium hypochlorite are generally around 0.1 mg/litre, although concentrations above 1 mg/litre have been reported. With chlorine dioxide disinfection, the concentration of chlorate depends heavily on process conditions (in both the chlorine dioxide generator and the water treatment plant) and applied dose of chlorine dioxide. As there is no viable option for reducing chlorate concentrations, control of chlorate concentration must rely on preventing its addition (from sodium hypochlorite) or formation (from chlorine dioxide). Chlorite ion is an inevitable by-product arising from the use of chlorine dioxide. When chlorine dioxide is used as the final disinfectant at typical doses, the resulting chlorite concentration should be <0.2 mg/litre. If chlorine dioxide is used as a pre-oxidant, the resulting chlorite concentration may need to be reduced using ferrous iron or activated carbon.
Guideline derivation	
• allocation to water	80% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorine dioxide

Chlorine dioxide has been shown to impair neurobehavioural and neurological development in rats exposed perinatally. Significant depression of thyroid hormones has also been observed in rats and monkeys exposed to it in drinking-water studies. A guideline value has not been established for chlorine dioxide because of its rapid hydrolysis to chlorite and because the chlorite provisional guideline value is adequately protective for potential toxicity from chlorine dioxide. The taste and odour threshold for this compound is 0.4 mg/litre.

Chlorite

IARC has concluded that chlorite is not classifiable as to its carcinogenicity to humans. The primary and most consistent finding arising from exposure to chlorite is oxidative stress resulting in changes in the red blood cells. This end-point is seen in laboratory animals and, by analogy with chlorate, in humans exposed to high doses in poisoning incidents. Studies with human volunteers for up to 12 weeks did not identify any effect on blood parameters at the highest dose tested, 36 µg/kg of body weight per day.

Chlorate

Like chlorite, the primary concern with chlorate is oxidative damage to red blood cells. Also like chlorite, a chlorate dose of 36 µg/kg of body weight per day for 12 weeks did not result in any adverse effects in human volunteers. Although the database for chlorate is less extensive than that for chlorite, a recent well conducted 90-day study in rats is available. A long-term study is in progress, which should provide more information on chronic exposure to chlorate.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chlorine dioxide, chlorate or chlorite. The 1993 Guidelines established a provisional health-based guideline value of 0.2 mg/litre for chlorite in drinking-water. The guideline value was designated as provisional because use of chlorine dioxide as a disinfectant may result in the chlorite guideline value being exceeded, and difficulties in meeting the guideline value must never be a reason for compromising disinfection. The 1993 Guidelines did not establish a health-based guideline value for chlorine dioxide in drinking-water because of its rapid breakdown and because the provisional guideline value for chlorite is adequately protective for potential toxicity from chlorine dioxide. The 1993 Guidelines concluded that available data on the effects of chlorate in humans and experimental animals are insufficient to permit development of a guideline value and recommended that further research was needed to characterize the non-lethal effects of chlorate. It was noted that the taste and odour threshold for chlorine dioxide is 0.4 mg/litre.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2000) *Disinfectants and disinfectant by-products.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2003) *Chlorite and chlorate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/86).

12.25 Chloroacetones

1,1-Dichloroacetone is formed from the reaction between chlorine and organic precursors and has been detected in chlorinated drinking-water. Concentrations are estimated to be less than 10 µg/litre and usually less than 1 µg/litre.

The toxicological data on 1,1-dichloroacetone are very limited, although studies with single doses indicate that it affects the liver.

There are insufficient data at present to permit the proposal of guideline values for 1,1-dichloroacetone or any of the other chloroacetones.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chloroacetones. The 1993 Guidelines concluded that there were insufficient data available to permit the proposal of guideline values for any of the chloroacetones.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chloroacetones in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/50).

12.26 Chlorophenols (2-chlorophenol, 2,4-dichlorophenol, 2,4,6-trichlorophenol)

Chlorophenols are present in drinking-water as a result of the chlorination of phenols, as by-products of the reaction of hypochlorite with phenolic acids, as biocides or as degradation products of phenoxy herbicides. Those most likely to occur in drinking-water as by-products of chlorination are 2-chlorophenol, 2,4-dichlorophenol and 2,4,6-trichlorophenol. The taste thresholds for chlorophenols in drinking-water are low.

Guideline value for 2,4,6-trichlorophenol	0.2 mg/litre
Occurrence	Concentrations of chlorophenols in drinking-water are usually less than 1 µg/litre.
Basis of guideline derivation	Applying the linearized multistage model to leukaemias in male rats observed in a 2-year feeding study (hepatic tumours found in this study were not used for risk estimation because of the possible role of contaminants in their induction)
Limit of detection	0.5–5 µg/litre by formation of pentafluorobenzyl ether derivatives; 1–10 µg/litre (monochlorophenols), 0.5 µg/litre (dichlorophenols) and 0.01 µg/litre (trichlorophenols) using GC with ECD
Treatment achievability	2,4,6-Trichlorophenol concentrations are generally less than 1 µg/litre. If necessary, 2,4,6-trichlorophenol concentrations can be reduced using GAC.
Additional comments	The guideline value for 2,4,6-trichlorophenol exceeds its lowest reported taste threshold.

Toxicological review

2-Chlorophenol

Data on the toxicity of 2-chlorophenol are limited. Therefore, no health-based guideline value has been derived.

2,4-Dichlorophenol

Data on the toxicity of 2,4-dichlorophenol are limited. Therefore, no health-based guideline value has been derived.

2,4,6-Trichlorophenol

2,4,6-Trichlorophenol has been reported to induce lymphomas and leukaemias in male rats and hepatic tumours in male and female mice. The compound has not been shown to be mutagenic in the Ames test but has shown weak mutagenic activity in other *in vitro* and *in vivo* studies. IARC has classified 2,4,6-trichlorophenol in Group 2B.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to chlorophenols. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline values for 2-chlorophenol, 4-chlorophenol, 2,4-dichlorophenol, 2,6-dichlorophenol or 2,4,5-trichlorophenol were recommended after a detailed evaluation of the compounds, although it was suggested that individual chlorophenols should not be present in drinking-water at a level above 0.0001 mg/litre for organoleptic reasons (and the total phenol content of water to be chlorinated should be kept below 0.001 mg/litre). In the same edition, a health-based guideline value of 0.01 mg/litre was recommended for 2,4,6-trichlorophenol, while noting

that the linear multistage extrapolation model appropriate for chemical carcinogens that was used in its derivation involved considerable uncertainty. It was also noted that 2,4,6-trichlorophenol may be detected by its taste and odour at a concentration of 0.0001 mg/litre. No health-based guidelines for 2-chlorophenol or 2,4-dichlorophenol were derived in the 1993 Guidelines, as data on their toxicity were limited. A guideline value of 0.2 mg/litre, associated with a 10^{-5} upper-bound excess lifetime cancer risk, was calculated for 2,4,6-trichlorophenol. This concentration exceeds the lowest reported taste threshold for the chemical (0.002 mg/litre).

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenols in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/47).

12.27 Chloropicrin

Chloropicrin, or trichloronitromethane, is formed by the reaction of chlorine with humic and amino acids and with nitrophenols. Its formation is increased in the presence of nitrates. Limited data from the USA indicate that concentrations in drinking-water are usually less than 5 µg/litre.

Decreased survival and body weights have been reported following long-term oral exposure in laboratory animals. Chloropicrin has been shown to be mutagenic in bacterial tests and in *in vitro* assays in lymphocytes. Because of the high mortality in a carcinogenesis bioassay and the limited number of end-points examined in the 78-week toxicity study, the available data were considered inadequate to permit the establishment of a guideline value for chloropicrin.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chloropicrin. The 1993 Guidelines considered the available data to be inadequate to permit the establishment of a guideline value for chloropicrin in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chloropicrin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/52).

12.28 Chlorotoluron

Chlorotoluron (CAS No. 15545-48-9) is a pre- or early post-emergence herbicide that is slowly biodegradable and mobile in soil. There is only very limited exposure to this compound from food.

Guideline value	0.03 mg/litre
Occurrence	Detected in drinking-water at concentrations of less than 1 µg/litre
TDI	11.3 µg/kg of body weight, derived from a NOAEL of 11.3 mg/kg of body weight per day for systemic effects in a 2-year feeding study in mice using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for evidence of carcinogenicity)
Limit of detection	0.1 µg/litre by separation by reverse-phase HPLC followed by UV and electrochemical detection
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorotoluron is of low toxicity in single, short-term and long-term exposures in animals, but it has been shown to cause an increase in adenomas and carcinomas of the kidneys of male mice given high doses for 2 years. As no carcinogenic effects were reported in a 2-year study in rats, it has been suggested that chlorotoluron has a carcinogenic potential that is both species- and sex-specific. Chlorotoluron and its metabolites have shown no evidence of genotoxicity.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorotoluron, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Chlorotoluron was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.03 mg/litre for chlorotoluron in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorotoluron in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/33).

12.29 Chlorpyrifos

Chlorpyrifos (CAS No. 2921-88-2) is a broad-spectrum organophosphorus insecticide used for the control of mosquitos, flies, various crop pests in soil and on foliage, household pests and aquatic larvae. Athough it is not recommended for addition to water for public health purposes by WHOPES, it may be used in some countries as an aquatic larvicide for the control of mosquito larvae. Chlorpyrifos is strongly absorbed by soil and does not readily leach from it, degrading slowly by microbial action. It has a low solubility in water and great tendency to partition from aqueous into organic phases in the environment.

Guideline value	0.03 mg/litre
Occurrence	Detected in surface waters in USA, usually at concentrations below 0.1 µg/litre; also detected in groundwater in less than 1% of the wells tested, usually at concentrations below 0.01 µg/litre
ADI	0.01 mg/kg of body weight on the basis of a NOAEL of 1 mg/kg of body weight per day for inhibition of brain acetylcholinesterase activity in studies in mice, rats and dogs, using a 100-fold uncertainty factor, and on the basis of a NOAEL of 0.1 mg/kg of body weight per day for inhibition of erythrocyte acetylcholinesterase activity in a study of human subjects exposed for 9 days, using a 10-fold uncertainty factor
Limit of detection	1 µg/litre by GC using an ECD or flame photometric detection
Treatment achievability	No data available; should be amenable to treatment by coagulation (10–20% removal), activated carbon adsorption and ozonation
Guideline derivation	
• allocation to water	10% of ADI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

JMPR concluded that chlorpyrifos is unlikely to pose a carcinogenic risk to humans. Chlorpyrifos was not genotoxic in an adequate range of studies *in vitro* and *in vivo*. In long-term studies, inhibition of cholinesterase activity was the main toxicological finding in all species.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorpyrifos, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Chlorpyrifos was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2000) *Pesticide residues in food – 1999 evaluations. Part II – Toxicological.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/00.4).

WHO (2003) *Chlorpyrifos in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/87).

12.30 Chromium

Chromium is widely distributed in the Earth's crust. It can exist in valences of +2 to +6. In general, food appears to be the major source of intake.

Provisional guideline value	0.05 mg/litre for total chromium The guideline value is designated as provisional because of uncertainties in the toxicological database.
Occurrence	Total chromium concentrations in drinking-water are usually less than 2 µg/litre, although concentrations as high as 120 µg/litre have been reported.
Basis of guideline value derivation	There are no adequate toxicity studies available to provide a basis for a NOAEL. The guideline value was first proposed in 1958 for hexavalent chromium, based on health concerns, but was later changed to a guideline for total chromium because of difficulties in analysing for the hexavalent form only.
Limit of detection	0.05–0.2 µg/litre for total chromium by AAS
Treatment achievability	0.015 mg/litre should be achievable using coagulation

Toxicological review

In a long-term carcinogenicity study in rats given chromium(III) by the oral route, no increase in tumour incidence was observed. In rats, chromium(VI) is a carcinogen via the inhalation route, although the limited data available do not show evidence

for carcinogenicity via the oral route. In epidemiological studies, an association has been found between exposure to chromium(VI) by the inhalation route and lung cancer. IARC has classified chromium(VI) in Group 1 (human carcinogen) and chromium(III) in Group 3. Chromium(VI) compounds are active in a wide range of *in vitro* and *in vivo* genotoxicity tests, whereas chromium(III) compounds are not.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.05 mg/litre for chromium (hexavalent), based on health concerns. This value was retained in the 1963 International Standards. Chromium was not evaluated in the 1971 International Standards. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, the guideline value of 0.05 mg/litre for total chromium was retained; total chromium was specified because of difficulties in analysing for the hexavalent form only. The 1993 Guidelines questioned the guideline value of 0.05 mg/litre because of the carcinogenicity of hexavalent chromium by the inhalation route and its genotoxicity, although the available toxicological data did not support the derivation of a new value. As a practical measure, 0.05 mg/litre, which is considered to be unlikely to give rise to significant health risks, was retained as the provisional guideline value until additional information becomes available and chromium can be re-evaluated.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chromium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/4).

12.31 Copper

Copper is both an essential nutrient and a drinking-water contaminant. It has many commercial uses. It is used to make pipes, valves and fittings and is present in alloys and coatings. Copper sulfate pentahydrate is sometimes added to surface water for the control of algae. Copper concentrations in drinking-water vary widely, with the primary source most often being the corrosion of interior copper plumbing. Levels in running or fully flushed water tend to be low, whereas those in standing or partially flushed water samples are more variable and can be substantially higher (frequently > 1 mg/litre). Copper concentrations in treated water often increase during distribution, especially in systems with an acid pH or high-carbonate waters with an alkaline pH. Food and water are the primary sources of copper exposure in developed

countries. Consumption of standing or partially flushed water from a distribution system that includes copper pipes or fittings can considerably increase total daily copper exposure, especially for infants fed formula reconstituted with tap water.

Guideline value	2 mg/litre
Occurrence	Concentrations in drinking-water range from ≤0.005 to >30 mg/litre, primarily as a result of the corrosion of interior copper plumbing.
Basis of guideline derivation	To be protective against acute gastrointestinal effects of copper and provide an adequate margin of safety in populations with normal copper homeostasis
Limit of detection	0.02–0.1 µg/litre by ICP/MS; 0.3 µg/litre by ICP/optical emission spectroscopy; 0.5 µg/litre by FAAS
Treatment achievability	Copper is not removed by conventional treatment processes. However, copper is not normally a raw water contaminant.
Additional comments	• For adults with normal copper homeostasis, the guideline value should permit consumption of 2 or 3 litres of water per day, use of a nutritional supplement and copper from foods without exceeding the tolerable upper intake level of 10 mg/day or eliciting an adverse gastrointestinal response. • Staining of laundry and sanitary ware occurs at copper concentrations above 1 mg/litre. At levels above 2.5 mg/litre, copper imparts an undesirable bitter taste to water; at higher levels, the colour of water is also impacted. • In most instances where copper tubing is used as a plumbing material, concentrations of copper will be below the guideline value. However, there are some conditions, such as highly acidic or aggressive waters, that will give rise to much higher copper concentrations, and the use of copper tubing may not be appropriate in such circumstances.

Toxicological review

IPCS concluded that the upper limit of the acceptable range of oral intake in adults is uncertain but is most likely in the range of several (more than 2 or 3) but not many milligrams per day in adults. This evaluation was based solely on studies of gastrointestinal effects of copper-contaminated drinking-water. The available data on toxicity in animals were not considered helpful in establishing the upper limit of the acceptable range of oral intake due to uncertainty about an appropriate model for humans, but they help to establish a mode of action for the response. The data on the gastrointestinal effects of copper must be used with caution, since the effects observed are influenced by the concentration of ingested copper to a greater extent than the total mass or dose ingested in a 24-h period. Recent studies have delineated the threshold for the effects of copper in drinking-water on the gastrointestinal tract, but there is still some uncertainty regarding the long-term effects of copper on sensitive populations, such as carriers of the gene for Wilson disease and other metabolic disorders of copper homeostasis.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of copper greater than 1.5 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 1.0 mg/litre was established for copper, based on its laundry and other staining properties. The 1993 Guidelines derived a provisional health-based guideline value of 2 mg/litre for copper from the PMTDI proposed by JECFA, based on a rather old study in dogs that did not take into account differences in copper metabolism between infants and adults. The guideline value was considered provisional because of the uncertainties regarding copper toxicity in humans. This guideline value was retained in the addendum to the Guidelines published in 1998 and remained provisional as a result of uncertainties in the dose–response relationship between copper in drinking-water and acute gastrointestinal effects in humans. It was stressed that the outcome of epidemiological studies in progress in Chile, Sweden and the USA may permit more accurate quantification of effect levels for copper-induced toxicity in humans, including sensitive subpopulations. Copper can also give rise to taste problems at concentrations above 5 mg/litre and can stain laundry and sanitary ware at concentrations above 1 mg/litre.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1998) *Copper.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 200).

WHO (2003) *Copper in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/88).

12.32 Cyanazine

Cyanazine (CAS No. 21725-46-2) 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.

Guideline value	0.0006 mg/litre (0.6 µg/litre)
Occurrence	Has been detected in surface water and groundwater, usually at concentrations of a few micrograms per litre, although levels as high as 1.3 and 3.5 mg/litre have been measured in surface water and groundwater, respectively

TDI	0.198 µg/kg of body weight based on a NOAEL of 0.198 mg/kg of body weight for hyperactivity in male rats in a 2-year toxicity/carcinogenicity study, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for limited evidence of carcinogenicity)
Limit of detection	0.01 µg/litre by GC with MS
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

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 (cf. atrazine). Cyanazine is also teratogenic in Fischer 344 rats at dose levels of 25 mg/kg of body weight per day and higher.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to cyanazine, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value for triazine herbicides, which include cyanazine, was recommended after a detailed evaluation of the compounds. Cyanazine was not evaluated in the second edition of the *Guidelines for Drinking-water Quality*, published in 1993. In the addendum to the second edition of these Guidelines, published in 1998, a health-based guideline value of 0.6 µg/litre was established for cyanazine in drinking-water.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Cyanazine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/60).

12.33 Cyanide

Cyanides can be found in some foods, particularly in some developing countries, and they are occasionally found in drinking-water, primarily as a consequence of industrial contamination.

Guideline value	0.07 mg/litre
Occurrence	Occasionally found in drinking-water
TDI	12 µg/kg of body weight, based on a LOAEL of 1.2 mg/kg of body weight per day for effects on behavioural patterns and serum biochemistry in a 6-month study in pigs, using an uncertainty factor of 100 for inter- and intraspecies variation (no additional factor for use of a LOAEL instead of a NOAEL was considered necessary because of doubts over the biological significance of the observed changes)
Limit of detection	2 µg/litre by titrimetric and photometric techniques
Treatment achievability	Cyanide is removed from water by high doses of chlorine.
Guideline derivation	
• allocation to water	20% of TDI (because exposure to cyanide from other sources is normally small and because exposure from water is only intermittent)
• weight	60-kg adult
• consumption	2 litres/day
Additional considerations	The guideline value is considered to be protective for acute and long-term exposure.

Toxicological review

The acute toxicity of cyanides is high. Effects on the thyroid and particularly the nervous system were observed in some populations as a consequence of the long-term consumption of inadequately processed cassava containing high levels of cyanide.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.01 mg/litre for cyanide, based on health concerns. This value was raised to 0.2 mg/litre in the 1963 International Standards. The tentative upper concentration limit was lowered to 0.05 mg/litre in the 1971 International Standards upon consideration of the ADI of hydrogen cyanide residues in some fumigated foods of 0.05 mg/kg of body weight and to ensure that the water source is not too highly contaminated by industrial effluents and that water treatment has been adequate. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was determined that a guideline value of 0.1 mg/litre would be a reasonable level for the protection of public health. A health-based guideline value of 0.07 mg/litre, which was considered to be protective for both acute and long-term exposure, was derived in the 1993 Guidelines.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Cyanide in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/5).

12.34 Cyanogen chloride

Cyanogen chloride is a by-product of chloramination. It is a reaction product of organic precursors with hypochlorous acid in the presence of ammonium ion. Concentrations detected in drinking-water treated with chlorine and chloramine were 0.4 and 1.6 µg/litre, respectively.

Cyanogen chloride is rapidly metabolized to cyanide in the body. There are few data on the oral toxicity of cyanogen chloride, and the guideline value is based, therefore, on cyanide. The guideline value is 70 µg/litre for cyanide as total cyanogenic compounds (see Cyanide in section 12.33).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to cyanogen chloride. The 1993 Guidelines derived a health-based guideline value for cyanogen chloride based on cyanide, as cyanogen chloride is rapidly metabolized to cyanide in the body and as there are few data on the oral toxicity of cyanogen chloride. The guideline value is 0.07 mg/litre for cyanide as total cyanogenic compounds (see Cyanide in section 12.33).

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Cyanogen chloride in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/51).

12.35 2,4-D (2,4-dichlorophenoxyacetic acid)

The term 2,4-D is used here to refer to the free acid, 2,4-dichlorophenoxyacetic acid (CAS No. 94-75-7). 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. 2,4-D is rapidly biodegraded in the environment. Residues of 2,4-D in food rarely exceed a few tens of micrograms per kilogram.

Guideline value	0.03 mg/litre
Occurrence	Levels in water usually below 0.5 µg/litre, although concentrations as high as 30 µg/litre have been measured
ADI	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 (for a variety of effects, including histopathological lesions in kidneys and liver) and a 2-year study of toxicity and carcinogenicity in rats (for renal lesions)
Limit of detection	0.1 µg/litre by gas–liquid chromatography with electrolytic conductivity detection
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 10% of ADI 60-kg adult 2 litres/day
Additional comments	The guideline value applies to 2,4-D, as salts and esters of 2,4-D are rapidly hydrolysed to the free acid in water

Toxicological review

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 was potentially contaminated with dioxins. JMPR concluded that it was not possible to evaluate the carcinogenic potential of 2,4-D on the basis of the available epidemiological studies. JMPR has also concluded that 2,4-D and its salts and esters are not genotoxic. The toxicity of the salts and esters of 2,4-D is comparable to that of the acid.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 2,4-D, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guide-*

lines for Drinking-water Quality, published in 1984, a health-based guideline value of 0.1 mg/litre was recommended for 2,4-D, based on the ADI recommended by WHO in 1976, but it was noted that some individuals may be able to detect 2,4-D by taste and odour at levels exceeding 0.05 mg/litre. The 1993 Guidelines established a health-based guideline value of 0.03 mg/litre for 2,4-D in drinking-water. This guideline value was retained in the addendum to these Guidelines, published in 1998, but was based on the more recent (1996) 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.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal references

FAO/WHO (1997) *Pesticide residues in food – 1996. Evaluations 1996. Part II – Toxicological.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/97.1).

WHO (2003) *2,4-D in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/70).

12.36 2,4-DB

The half-lives for degradation of chlorophenoxy herbicides, including 2,4-DB (CAS No. 94-82-6), in the environment are in the order of several days. Chlorophenoxy herbicides are not often found in food.

Guideline value	0.09 mg/litre
Occurrence	Chlorophenoxy herbicides not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre
TDI	30 µg/kg of body weight, based on a NOAEL of 3 mg/kg of body weight per day for effects on body and organ weights, blood chemistry and haematological parameters in a 2-year study in rats, with an uncertainty factor of 100 (for inter- and intraspecies variation)
Limit of detection	1 µg/litre to 1 mg/litre for various methods commonly used for the determination of chlorophenoxy herbicides in water, including solvent extraction, separation by GC, gas–liquid chromatography, thin-layer chromatography or HPLC, with ECD or UV detection
Treatment achievability	0.1 µg/litre should be achievable using GAC

Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional considerations	The NOAEL used in the guideline value derivation is similar to the NOAEL of 2.5 mg/kg of body weight per day obtained in a short-term study in beagle dogs and the NOAEL for hepatocyte hypertrophy of 5 mg/kg of body weight per day obtained in a 3-month study in rats.

Toxicological review

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, the available data from studies in exposed populations and animals do not permit assessment of the carcinogenic potential to humans of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorophenoxy herbicides, including 2,4-DB, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 2,4-DB was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.09 mg/litre for 2,4-DB.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/44).

12.37 DDT and metabolites

The structure of DDT (CAS No. 107917-42-0) permits several different isomeric forms, and commercial products consist predominantly of *p*,*p*'-DDT. Its use has been restricted or banned in several countries, although DDT is still used in some countries for the control of vectors that transmit yellow fever, sleeping sickness, typhus, malaria and other insect-transmitted diseases. DDT and its metabolites are persistent

in the environment and resistant to complete degradation by microorganisms. Food is the major source of intake of DDT and related compounds for the general population.

Guideline value	0.001 mg/litre
Occurrence	Detected in surface water at concentrations below 1 µg/litre; also detected in drinking-water at 100-fold lower concentrations
PTDI	0.01 mg/kg of body weight based on a NOAEL of 1 mg/kg of body weight per day for developmental toxicity in rats, applying an uncertainty factor of 100
Limit of detection	0.011 µg/litre by GC using an ECD
Treatment achievability	0.1 µg/litre should be achievable using coagulation or GAC
Guideline derivation • allocation to water • weight • consumption	 1% of PTDI 10-kg child 1 litre/day
Additional comments	• DDT is listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines. • The guideline value is derived on the basis of a 10-kg child consuming 1 litre of drinking-water per day, because infants and children may be exposed to greater amounts of chemicals in relation to their body weight and because of concern over the bioaccumulation of DDT. • It should be emphasized that the benefits of DDT use in malaria and other vector control programmes outweigh any health risk from the presence of DDT in drinking-water.

Toxicological review

A working group convened by IARC classified the DDT complex as a non-genotoxic carcinogen in rodents and a potent promoter of liver tumours. IARC has concluded that there is insufficient evidence in humans and sufficient evidence in experimental animals for the carcinogenicity of DDT (Group 2B) based upon liver tumours observed in rats and mice. The results of epidemiological studies of pancreatic cancer, multiple myeloma, non-Hodgkin lymphoma and uterine cancer did not support the hypothesis of an association with environmental exposure to the DDT complex. Conflicting data were obtained with regard to some genotoxic end-points. In most studies, DDT did not induce genotoxic effects in rodent or human cell systems, nor was it mutagenic to fungi or bacteria. The US Agency for Toxic Substances and Disease Registry concluded that the DDT complex could impair reproduction and/or development in several species. Hepatic effects of DDT in rats include increased liver weights, hypertrophy, hyperplasia, induction of microsomal enzymes, including cytochrome P450, cell necrosis, increased activity of serum liver enzymes and mitogenic effects, which might be related to a regenerative liver response to DDT.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to DDT, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.001 mg/litre was recommended for DDT (total isomers), based on the ADI recommended by JMPR in 1969. The 1993 Guidelines established a health-based guideline value of 0.002 mg/litre for DDT and its metabolites in drinking-water, derived from the ADI recommended by JMPR in 1984 and taking into consideration the fact that infants and children may be exposed to greater amounts of chemicals in relation to their body weight, concern over the bioaccumulation of DDT and the significant exposure to DDT by routes other than water. It was noted that the guideline value exceeds the water solubility of DDT of 0.001 mg/litre, but that some DDT may be adsorbed onto the small amount of particulate matter present in drinking-water, so the guideline value could be reached under certain circumstances. It was also emphasized that the benefits of DDT use in malaria and other vector control programmes far outweigh any health risk from the presence of DDT in drinking-water.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2001) *Pesticide residues in food – 2000. Evaluations – 2000. Part II – Toxicology.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/01.3).

WHO (2003) *DDT and its derivatives in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/89).

12.38 Dialkyltins

The group of chemicals known as the organotins is composed of a large number of compounds with differing properties and applications. The most widely used of the organotins are the disubstituted compounds, which are employed as stabilizers in plastics, including polyvinyl chloride (PVC) water pipes, and the trisubstituted compounds, which are widely used as biocides.

The disubstituted compounds that may leach from PVC water pipes at low concentrations for a short time after installation are primarily immunotoxins, although they appear to be of low general toxicity. The data available are insufficient to permit the proposal of guideline values for individual dialkyltins.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to dialkyltins. The 1993 Guidelines concluded that the data available were insufficient to permit the proposal of guideline values for individual dialkyltins.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Dialkyltins in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/109).

12.39 1,2-Dibromo-3-chloropropane (DBCP)

1,2-Dibromo-3-chloropropane (CAS No. 96-12-8) is a soil fumigant that is highly soluble in water. It has a taste and odour threshold in water of 10 µg/litre. DBCP was detected in vegetables grown in treated soils, and low levels have been detected in air.

Guideline value	0.001 mg/litre
Occurrence	Limited survey found levels of up to a few micrograms per litre in drinking-water
Basis of guideline derivation	Linearized multistage model was applied to the data on the incidence of stomach, kidney and liver tumours in the male rat in a 104-week dietary study
Limit of detection	0.02 µg/litre by GC with ECD
Treatment achievability	1 µg/litre should be achievable using air stripping followed by GAC
Additional comments	The guideline value of 1 µg/litre should be protective for the reproductive toxicity of DBCP.

Toxicological review

On the basis of animal data from different strains of rats and mice, DBCP was determined to be carcinogenic in both sexes by the oral, inhalation and dermal routes. DBCP was also determined to be a reproductive toxicant in humans and several species of laboratory animals. DBCP was found to be genotoxic in a majority of *in vitro* and *in vivo* assays. IARC has classified DBCP in Group 2B based upon sufficient evidence of carcinogenicity in animals. Recent epidemiological evidence suggests an increase in cancer mortality in individuals exposed to high levels of DBCP.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to DBCP, but the 1971 International Standards suggested that pesticide residues that may

occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. DBCP was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines calculated a guideline value of 0.001 mg/litre for DBCP in drinking-water, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5} and sufficiently protective for the reproductive toxicity of the pesticide. It was noted that for a contaminated water supply, extensive treatment would be required to reduce the level of DBCP to the guideline value.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,2-Dibromo-3-chloropropane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/34).

12.40 1,2-Dibromoethane (ethylene dibromide)

1,2-Dibromoethane (CAS No. 106-93-4) 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.

Provisional guideline value	0.0004 mg/litre (0.4 µg/litre) The guideline value is provisional due to serious limitations of the critical studies.
Occurrence	Detected in groundwater following its use as a soil fumigant at concentrations as high as 100 µg/litre
Basis of guideline derivation	Lower end of the range (and thus more conservative estimate) of lifetime low-dose cancer risks 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

Limit of detection	0.01 µg/litre by microextraction GC/MS; 0.03 µg/litre by purge and trap GC with halogen-specific detector; 0.8 µg/litre by purge-and-trap capillary column GC with photoionization and electrolytic conductivity detectors in series
Treatment achievability	0.1 µg/litre should be achievable using GAC

Toxicological review

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 of *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).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 1,2-dibromoethane, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 1,2-Dibromoethane was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines noted that 1,2-dibromoethane appears to be a genotoxic carcinogen. However, as the studies to date were inadequate for mathematical risk extrapolation, a guideline value for 1,2-dibromoethane was not derived. The Guidelines recommended that 1,2-dibromoethane be re-evaluated as soon as new data became available. In the addendum to these Guidelines, published in 1998, the guideline value that corresponds to an upper-bound excess lifetime cancer risk for various tumour types of 10^{-5} was calculated to be in the range 0.0004–0.015 mg/litre. This guideline value was considered to be provisional because of the serious limitations of the critical studies.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1995) *Report of the 1994 meeting of the Core Assessment Group*. Geneva, World Health Organization, International Programme on Chemical Safety, Joint Meeting on Pesticides (WHO/PCS/95.7).

IPCS (1996) *1,2-Dibromoethane*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 177).

WHO (2003) *1,2-Dibromoethane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/66).

12.41 Dichloroacetic acid

Chlorinated acetic acids, including dichloroacetic acid (DCA), are formed from organic material during water chlorination. DCA has been used as a therapeutic agent to treat lactic acidosis, diabetes and familial hyperlipidaemia in humans.

Provisional guideline value	0.05 mg/litre The guideline value is designated as provisional because the data on treatment are insufficient to ensure that the health-based value of 0.04 mg/litre is technically achievable in a wide range of circumstances. Difficulties in meeting a guideline value must never be a reason to compromise adequate disinfection.
Occurrence	Found in groundwater and surface water distribution systems at concentrations up to about 100 µg/litre, with mean concentrations below 20 µg/litre
Basis of guideline derivation	Using the tumour prevalence data from male mice, the combined data for carcinomas and adenomas in male B6C3F1 mice exposed to doses of 0, 8, 84, 168, 315 or 429 mg/kg of body weight per day for up to 2 years were plotted using the US EPA's Benchmark Dose software version 1.3.1. The slope factor of 0.0075 (mg/kg of body weight per day)$^{-1}$ was derived from the $BMDL_{10}$ using a linear multistage model of the dose–response data.
Limit of detection	<0.1–0.4 µg/litre by GC with ECD; practical quantification level 1 µg/litre
Treatment achievability	Concentrations may be reduced by installing or optimizing coagulation to remove precursors and/or by controlling the pH during chlorination.
Additional comments	The concentration associated with a 10^{-5} upper-bound excess lifetime cancer risk is 40 µg/litre. However, it may not be possible to adequately disinfect potable water and maintain DCA levels below 40 µg/litre, so the provisional guideline value of 50 µg/litre is retained.

Toxicological review

IARC reclassified DCA as Group 2B (possibly carcinogenic to humans) in 2002, based on the absence of data on human carcinogenicity and sufficient evidence of its carcinogenicity in experimental animals. This classification was based primarily on findings of liver tumours in rats and mice. Genotoxicity data are considered to be inconclusive, particularly at lower doses. Glycogen deposition, peroxisome proliferation, changes in signal transduction pathways and DNA hypomethylation have all been observed following DCA exposure and have been hypothesized to be involved in its carcinogenicity. However, the available data are not sufficient to establish a cancer mode of action with reasonable certainty, especially at the very low exposure levels expected to apply to humans ingesting chlorinated drinking-water. Recent data suggest that there may be more than one mechanism leading to tumours, since altered hepatic foci from treated mice were found to have three different types of cellular characteristics.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to DCA. In the 1993 Guidelines, a provisional guideline value of 0.05 mg/litre was derived for DCA; the guideline value was designated as provisional because the data were insufficient to ensure that the value was technically achievable. This guideline value was brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal reference

WHO (2005) *Dichloroacetic acid in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/121).

12.42 Dichlorobenzenes (1,2-dichlorobenzene, 1,3-dichlorobenzene, 1,4-dichlorobenzene)

The dichlorobenzenes (DCBs) are widely used in industry and in domestic products such as odour-masking agents, chemical dyestuffs and pesticides. Sources of human exposure are predominantly air and food.

Guideline values	
1,2-Dichlorobenzene	1 mg/litre
1,4-Dichlorobenzene	0.3 mg/litre

Occurrence	Have been found in raw water sources at levels as high as 10 µg/litre and in drinking-water at concentrations up to 3 µg/litre; much higher concentrations (up to 7 mg/litre) present in contaminated groundwater
TDIs	
1,2-Dichlorobenzene	429 µg/kg of body weight, based on a NOAEL of 60 mg/kg of body weight per day for tubular degeneration of the kidney identified in a 2-year mouse gavage study, correcting for 5 days per week dosing and using an uncertainty factor of 100 (for inter- and intraspecies variation)
1,4-Dichlorobenzene	107 µg/kg of body weight, based on a LOAEL of 150 mg/kg of body weight per day for kidney effects identified in a 2-year rat study, correcting for 5 days per week dosing and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the use of a LOAEL instead of a NOAEL and the carcinogenicity end-point)

Limit of detection	0.01–0.25 µg/litre by gas–liquid chromatography with ECD; 3.5 µg/litre by GC using a photoionization detector
Treatment achievability	0.01 mg/litre should be achievable using air stripping
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	Guideline values for both 1,2- and 1,4-DCB far exceed their lowest reported taste thresholds in water of 1 and 6 µg/litre, respectively.

Toxicological review

1,2-Dichlorobenzene

1,2-DCB is of low acute toxicity by the oral route of exposure. Oral exposure to high doses of 1,2-DCB affects mainly the liver and kidneys. The balance of evidence suggests that 1,2-DCB is not genotoxic, and there is no evidence for its carcinogenicity in rodents.

1,3-Dichlorobenzene

There are insufficient toxicological data on this compound to permit a guideline value to be proposed, but it should be noted that it is rarely found in drinking-water.

1,4-Dichlorobenzene

1,4-DCB is of low acute toxicity, but there is evidence that it increases the incidence of renal tumours in rats and of hepatocellular adenomas and carcinomas in mice after long-term exposure. IARC has placed 1,4-DCB in Group 2B. 1,4-DCB is not considered to be genotoxic, and the relevance for humans of the tumours observed in animals is doubtful.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to DCBs. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended for 1,2- or 1,4-DCB after a detailed evaluation of the compounds. Toxicological limits for drinking-water of 0.005–0.05 mg/litre were derived based on an ADI; given that the threshold odour concentrations are 0.003 mg/litre for 1,2-DCB and 0.001 mg/litre for 1,4-DCB, 10% of each of these values was recommended as a level unlikely to give rise to taste and odour problems in drinking-water supplies. The 1993 Guidelines calculated a health-based guideline value of 1 mg/litre for 1,2-DCB, which far exceeds the lowest reported taste threshold of 1,2-DCB in water (0.001 mg/litre). There were insufficient toxicological data on 1,3-DCB to permit a guideline value to be proposed, but the 1993 Guidelines noted that it is rarely found in drinking-water. A health-based guideline value of 0.3 mg/litre was proposed for 1,4-DCB, which far exceeds the lowest reported odour threshold of 1,4-DCB in water (0.0003 mg/litre).

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Dichlorobenzenes in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/28).

12.43 1,1-Dichloroethane

1,1-Dichloroethane is used as a chemical intermediate and solvent. There are limited data showing that it can be present at concentrations of up to 10 µg/litre in drinking-water. However, because of the widespread use and disposal of this chemical, its occurrence in groundwater may increase.

1,1-Dichloroethane is rapidly metabolized by mammals to acetic acid and a variety of chlorinated compounds. It is of relatively low acute toxicity, and limited data are available on its toxicity from short- and long-term studies. There is limited *in vitro* evidence of genotoxicity. One carcinogenicity study by gavage in mice and rats provided no conclusive evidence of carcinogenicity, although there was some evidence of an increased incidence of haemangiosarcomas in treated animals.

In view of the very limited database on toxicity and carcinogenicity, it was concluded that no guideline value should be proposed.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to 1,1-dichloroethane. In view of the very limited database on toxicity and carcinogenicity, the 1993 Guidelines concluded that no guideline value for 1,1-dichloroethane should be proposed.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,1-Dichloroethane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/19).

12.44 1,2-Dichloroethane

1,2-Dichloroethane is used mainly as an intermediate in the production of vinyl chloride and other chemicals and to a lesser extent as a solvent. It may enter surface waters via effluents from industries that manufacture or use the substance. It may also enter groundwater, where it may persist for long periods, following disposal in waste sites. It is found in urban air.

Guideline value	0.030 mg/litre
Occurrence	Has been found in drinking-water at levels of up to a few micrograms per litre
Basis of guideline derivation	Applying the linearized multistage model to haemangiosarcomas observed in male rats in a 78-week gavage study
Limit of detection	0.06–2.8 µg/litre by GC/MS; 0.03–0.2 µg/litre by GC with electrolytic conductivity detector; 5 µg/litre by GC with FID; 0.03 µg/litre by GC with photoionization detection
Treatment achievability	0.0001 mg/litre should be achievable using GAC
Additional considerations	The guideline value of 0.030 mg/litre is consistent with the value derived from IPCS (1998), based on a 10^{-5} risk level.

Toxicological review

IARC has classified 1,2-dichloroethane in Group 2B (possible human carcinogen). It has been shown to produce statistically significant increases in a number of tumour types in laboratory animals, including the relatively rare haemangiosarcoma, and the balance of evidence indicates that it is potentially genotoxic. Targets of 1,2-dichloroethane toxicity in orally exposed animals included the immune system, central nervous system, liver and kidney. Data indicate that 1,2-dichloroethane is less potent when inhaled.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to 1,2-dichloroethane. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.01 mg/litre was recommended for 1,2-dichloroethane, while noting that the mathematical model appropriate to chemical carcinogens that was used in its derivation involved considerable uncertainty. The 1993 Guidelines calculated a guideline value of 0.03 mg/litre for 1,2-dichloroethane on the basis of haemangiosarcomas observed in male rats, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5}.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1995) *1,2-Dichloroethane*, 2nd ed. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 176).

IPCS (1998) *1,2-Dichloroethane*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 1).

WHO (2003) *1,2-Dichloroethane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/67).

12.45 1,1-Dichloroethene

1,1-Dichloroethene, or vinylidene chloride, is used mainly as a monomer in the production of polyvinylidene chloride co-polymers and as an intermediate in the synthesis of other organic chemicals. It is an occasional contaminant of drinking-water, usually being found together with other chlorinated hydrocarbons. There are no data on levels in food, but levels in air are generally less than 40 ng/m^3 except at some manufacturing sites. 1,1-Dichloroethene is detected in finished drinking-water taken from groundwater sources at median concentrations of 0.28–1.2 µg/litre and in public drinking-water supplies at concentrations ranging from ≤0.2 to 0.5 µg/litre.

1,1-Dichloroethene is a central nervous system depressant and may cause liver and kidney toxicity in occupationally exposed humans. It causes liver and kidney damage in laboratory animals. IARC has placed 1,1-dichloroethene in Group 3. It was found to be genotoxic in a number of test systems *in vitro* but was not active in the dominant lethal and micronucleus assays *in vivo*. It induced kidney tumours in mice in one inhalation study but was reported not to be carcinogenic in a number of other studies, including several in which it was given in drinking-water.

A health-based value of 140 µg/litre (rounded value) can be derived from a TDI of 0.046 mg/kg of body weight, derived using the BMD approach from a study in which the critical effect was minimal hepatocellular mid-zonal fatty change in female rats. However, this value is significantly higher than the concentrations of 1,1-dichloroethene normally found in drinking-water. It is therefore considered unnecessary to set a formal guideline value for 1,1-dichloroethene in drinking-water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to 1,1-dichloroethene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.0003 mg/litre was recommended for 1,1-dichloroethene, while noting that the mathematical model appropriate to chemical carcinogens that was used in its derivation involved considerable uncertainty. A health-based guideline value of 0.03 mg/litre for 1,1-dichloroethene was recommended in the 1993 Guidelines. This value was brought forward to the third edition of the Guidelines.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (2003) *1,1-Dichloroethene (vinylidene chloride)*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 51).

WHO (2005) *1,1-Dichloroethene in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/20).

12.46 1,2-Dichloroethene

1,2-Dichloroethene exists in a *cis* and a *trans* form. The *cis* form is more frequently found as a water contaminant. The presence of these two isomers, which are metabolites of other unsaturated halogenated hydrocarbons in wastewater and anaerobic groundwater, may indicate the simultaneous presence of more toxic organochlorine chemicals, such as vinyl chloride. Accordingly, their presence indicates that more intensive monitoring should be conducted. There are no data on exposure from food. Concentrations in air are low, with higher concentrations, in the microgram per cubic metre range, near production sites. The *cis* isomer was previously used as an anaesthetic.

Guideline value	0.05 mg/litre
Occurrence	Has been found in drinking-water supplies derived from groundwater at levels up to 120 µg/litre
TDI	17 µg/kg of body weight, based on a NOAEL (for increases in serum alkaline phosphatase levels and increased thymus weight) of 17 mg/kg of body weight from a 90-day study in mice administered *trans*-1,2-dichloroethene in drinking-water, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the short duration of the study)
Limit of detection	0.17 µg/litre by GC with MS
Treatment achievability	0.01 mg/litre should be achievable using GAC or air stripping

Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	Data on the *trans* isomer were used to calculate a joint guideline value for both isomers because toxicity for the *trans* isomer occurred at a lower dose than for the *cis* isomer and because data suggest that the mouse is a more sensitive species than the rat.

Toxicological review

There is little information on the absorption, distribution and excretion of 1,2-dichloroethene. However, by analogy with 1,1-dichloroethene, it would be expected to be readily absorbed, distributed mainly to the liver, kidneys and lungs and rapidly excreted. The *cis* isomer is more rapidly metabolized than the *trans* isomer in *in vitro* systems. Both isomers have been reported to cause increased serum alkaline phosphatase levels in rodents. In a 3-month study in mice given the *trans* isomer in drinking-water, there was a reported increase in serum alkaline phosphatase and reduced thymus and lung weights. Transient immunological effects were also reported, the toxicological significance of which is unclear. *Trans*-1,2-dichloroethene also caused reduced kidney weights in rats, but at higher doses. Only one rat toxicity study is available for the *cis* isomer, which produced toxic effects in rats similar in magnitude to those induced by the *trans* isomer in mice, but at higher doses. There are limited data to suggest that both isomers may possess some genotoxic activity. There is no information on carcinogenicity.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to 1,2-dichloroethene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended after a detailed evaluation of the compound. In the 1993 Guidelines, a joint guideline value of 0.05 mg/litre was calculated for both 1,2-dichloroethene isomers using toxicity data on the *trans* isomer.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,2-Dichloroethene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/72).

12.47 Dichloromethane

Dichloromethane, or methylene chloride, is widely used as a solvent for many purposes, including coffee decaffeination and paint stripping. Exposure from drinking-water is likely to be insignificant compared with that from other sources.

Guideline value	0.02 mg/litre
Occurrence	Dichloromethane has been found in surface water samples at concentrations ranging from 0.1 to 743 µg/litre. Levels are usually higher in groundwater because volatilization is restricted; concentrations as high as 3600 µg/litre have been reported. Mean concentrations in drinking-water were less than 1 µg/litre.
TDI	6 µg/kg of body weight, derived from a NOAEL of 6 mg/kg of body weight per day for hepatotoxic effects in a 2-year drinking-water study in rats, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for concern about carcinogenic potential)
Limit of detection	0.3 µg/litre by purge-and-trap GC with MS detection (note that dichloromethane vapour readily penetrates tubing during the procedure)
Treatment achievability	20 µg/litre should be achievable using air stripping
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

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

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to dichloromethane. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended after a detailed evaluation of the compound. The 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for dichloromethane, noting that widespread exposure from other sources is possible.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Dichloromethane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/18).

12.48 1,2-Dichloropropane (1,2-DCP)

1,2-Dichloropropane (CAS No. 78-87-5) 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.

Provisional guideline value	0.04 mg/litre The guideline value is provisional owing to limitations of the toxicological database.
Occurrence	Detected in groundwater and drinking-water, usually at concentrations below 20 µg/litre, although levels as high as 440 µg/litre have been measured in well water
TDI	14 µg/kg of body weight based on a LOAEL of 71.4 mg/kg of body weight per day (100 mg/kg of body weight per day corrected for 5 days per week dosing) for changes in haematological parameters in a 13-week study in male rats, with an uncertainty factor of 5000 (100 for inter- and intraspecies variation, 10 for use of a LOAEL and 5 to reflect limitations of the database, including the limited data on *in vivo* genotoxicity and use of a subchronic study)
Limit of detection	0.02 µg/litre by a purge-and-trap GC method with an electrolytic conductivity detector or GC/MS
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day

Toxicological review

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 insufficient data with which 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.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 1,2-DCP, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 1,2-DCP was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines proposed a provisional health-based guideline value of 0.02 mg/litre for 1,2-DCP in drinking-water. The value was provisional because an uncertainty factor of 10 000 was used in its derivation. This guideline value was amended to 0.04 mg/litre in the addendum to these Guidelines, published in 1998, using a lower uncertainty factor. This guideline value was considered to be provisional owing to the magnitude of the uncertainty factor and the fact that the database had not changed since the previous guideline value had been derived.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,2-Dichloropropane (1,2-DCP) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/61).

12.49 1,3-Dichloropropane

1,3-Dichloropropane (CAS No. 142-28-9) has several industrial uses and may be found as a contaminant of soil fumigants containing 1,3-dichloropropene. It is rarely found in water.

1,3-Dichloropropane is of low acute toxicity. There is some indication that it may be genotoxic in bacterial systems. No short-term, long-term, reproductive or developmental toxicity data pertinent to exposure via drinking-water could be located in the literature. The available data are considered insufficient to permit recommendation of a guideline value.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 1,3-dichloropropane, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 1,3-Dichloropropane was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines concluded that the available data

were insufficient to permit recommendation of a guideline value for 1,3-dichloropropane in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,3-Dichloropropane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/35).

12.50 1,3-Dichloropropene

1,3-Dichloropropene (CAS Nos. 542-75-6 isomer mixture; 10061-01-5 *cis* isomer; 10061-02-6 *trans* isomer) is a soil fumigant, the commercial product being a mixture of *cis* and *trans* isomers. It is used to control a wide variety of soil pests, particularly nematodes in sandy soils. Notwithstanding its high vapour pressure, it is soluble in water at the gram per litre level and can be considered a potential water contaminant.

Guideline value	0.02 mg/litre
Occurrence	Has been found in surface water and groundwater at concentrations of a few micrograms per litre
Basis of guideline derivation	Calculated by applying the linearized multistage model to the observation of lung and bladder tumours in female mice in a 2-year gavage study
Limit of detection	0.34 and 0.20 µg/litre by purge-and-trap packed column GC using an electrolytic conductivity detector or microcoulometric detector for *cis*-1,3-dichloropropene and *trans*-1,3- dichloropropene, respectively
Treatment achievability	No information found on removal from water

Toxicological review

1,3-Dichloropropene is a direct-acting mutagen that has been shown to produce forestomach tumours following long-term oral gavage exposure in rats and mice. Tumours have also been found in the bladder and lungs of female mice and the liver of male rats. Long-term inhalation studies in the rat have proved negative, whereas some benign lung tumours have been reported in inhalation studies in mice. IARC has classified 1,3-dichloropropene in Group 2B (possible human carcinogen).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 1,3-dichloropropene, but the 1971 International Standards suggested that pesticide

residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 1,3-Dichloropropene was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines calculated a guideline value of 0.02 mg/litre for 1,3-dichloropropene in drinking-water, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5}.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *1,3-Dichloropropene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/36).

12.51 Dichlorprop (2,4-DP)

The half-lives for degradation of chlorophenoxy herbicides, including dichlorprop (CAS No. 120-36-5), in the environment are in the order of several days. Chlorophenoxy herbicides are not often found in food.

Guideline value	0.1 mg/litre
Occurrence	Chlorophenoxy herbicides not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre
TDI	36.4 µg/kg of body weight, based on a NOAEL for renal toxicity in a 2-year study in rats of 100 mg/kg of diet, equal to 3.64 mg/kg of body weight per day, applying an uncertainty factor of 100 (for intra- and interspecies variation)
Limit of detection	1 µg/litre to 1 mg/litre for various methods commonly used for the determination of chlorophenoxy herbicides in water, including solvent extraction, separation by GC, gas–liquid chromatography, thin-layer chromatography or HPLC, with ECD or UV detection
Treatment achievability	No data available
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, the available data from studies in exposed populations and animals do not

permit assessment of the carcinogenic potential to humans of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. In dietary studies in rats, slight liver hypertrophy was observed in a 3-month study, and effects in a 2-year study included hepatocellular swelling, mild anaemia, increased incidence of brown pigment in the kidneys (possibly indicative of slight degeneration of the tubular epithelium) and decreased urinary specific gravity and protein.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorophenoxy herbicides, including dichlorprop, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Dichlorprop was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.1 mg/litre for dichlorprop.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/44).

12.52 Di(2-ethylhexyl)adipate

Di(2-ethylhexyl)adipate (DEHA) is used mainly as a plasticizer for synthetic resins such as PVC. Reports of the presence of DEHA in surface water and drinking-water are scarce, but DEHA has occasionally been identified in drinking-water at levels of a few micrograms per litre. As a consequence of its use in PVC films, food is the most important source of human exposure (up to 20 mg/day).

DEHA is of low short-term toxicity; however, dietary levels above 6000 mg/kg of feed induce peroxisomal proliferation in the liver of rodents. This effect is often associated with the development of liver tumours. DEHA induced liver carcinomas in female mice at very high doses but not in male mice or rats. It is not genotoxic. IARC has placed DEHA in Group 3.

A health-based value of 80 µg/litre can be calculated for DEHA on the basis of a TDI of 280 µg/kg of body weight, based on fetotoxicity in rats, and allocating 1% of the TDI to drinking-water. However, because DEHA occurs at concentrations well

below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to DEHA. The 1993 Guidelines proposed a health-based guideline value of 0.08 mg/litre for DEHA in drinking-water.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Di(2-ethylhexyl)adipate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/68).

12.53 Di(2-ethylhexyl)phthalate

Di(2-ethylhexyl)phthalate (DEHP) is used primarily as a plasticizer. Exposure among individuals may vary considerably because of the broad nature of products into which DEHP is incorporated. In general, food will be the main exposure route.

Guideline value	0.008 mg/litre
Occurrence	Found in surface water, groundwater and drinking-water in concentrations of a few micrograms per litre; in polluted surface water and groundwater, concentrations of hundreds of micrograms per litre have been reported
TDI	25 µg/kg of body weight, based on a NOAEL of 2.5 mg/kg of body weight per day for peroxisomal proliferation in the liver in rats, using an uncertainty factor of 100 for inter- and Intraspecies variation
Limit of detection	0.1 µg/litre by GC/MS
Treatment achievability	No data available
Guideline derivation • allocation to water • weight • consumption	 1% of TDI 60-kg adult 2 litres/day
Additional comments	The reliability of some data on environmental water samples is questionable because of secondary contamination during sampling and working-up procedures. Concentrations that exceed the solubility more than 10-fold have been reported.

Toxicological review

In rats, DEHP is readily absorbed from the gastrointestinal tract. In primates (including humans), absorption after ingestion is lower. Species differences are also observed

in the metabolic profile. Most species excrete primarily the conjugated mono-ester in urine. Rats, however, predominantly excrete terminal oxidation products. DEHP is widely distributed in the body, with highest levels in liver and adipose tissue, without showing significant accumulation. The acute oral toxicity is low. The most striking effect in short-term toxicity studies is the proliferation of hepatic peroxisomes, indicated by increased peroxisomal enzyme activity and histopathological changes. The available information suggests that primates, including humans, are far less sensitive to this effect than rodents. In long-term oral carcinogenicity studies, hepatocellular carcinomas were found in rats and mice. IARC has concluded that DEHP is possibly carcinogenic to humans (Group 2B). In 1988, JECFA evaluated DEHP and recommended that human exposure to this compound in food be reduced to the lowest level attainable. The Committee considered that this might be achieved by using alternative plasticizers or alternatives to plastic material containing DEHP. In a variety of *in vitro* and *in vivo* studies, DEHP and its metabolites have shown no evidence of genotoxicity, with the exception of induction of aneuploidy and cell transformation.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to DEHP. The 1993 Guidelines established a health-based guideline value of 0.008 mg/litre for DEHP in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Di(2-ethylhexyl)phthalate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/29).

12.54 Dimethoate

Dimethoate (CAS No. 60-51-5) is an organophosphorus insecticide used to control a broad range of insects in agriculture, as well as the housefly. It has a half-life of 18 h to 8 weeks and is not expected to persist in water, although it is relatively stable at pH 2–7. A total daily intake from food of 0.001 µg/kg of body weight has been estimated.

Guideline value	0.006 mg/litre
Occurrence	Detected at trace levels in a private well in Canada, but not detected in a Canadian survey of surface water or drinking- water supplies
ADI	0.002 mg/kg of body weight based on an apparent NOAEL of 1.2 mg/kg of body weight per day for reproductive performance in a study of reproductive toxicity in rats, applying an uncertainty factor of 500 to take into consideration concern regarding whether this could be a LOAEL
Limit of detection	0.05 µg/litre by GC/MS
Treatment achievability	1 µg/litre should be achievable using GAC and chlorination
Guideline derivation	
• allocation to water	10% of ADI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

In studies with human volunteers, dimethoate has been shown to be a cholinesterase inhibitor and a skin irritant. Dimethoate is not carcinogenic to rodents. JMPR concluded that although *in vitro* studies indicate that dimethoate has mutagenic potential, this potential does not appear to be expressed in vivo. In a multigeneration study of reproductive toxicity in rats, the NOAEL appeared to be 1.2 mg/kg of body weight per day, but there was some indication that reproductive performance may have been affected at lower doses. No data were available to assess whether the effects on reproductive performance were secondary to inhibition of cholinesterase. JMPR concluded that it was not appropriate to base the ADI on the results of the studies of volunteers, since the crucial end-point (reproductive performance) has not been assessed in humans. It was suggested that there may be a need to re-evaluate the toxicity of dimethoate after the periodic review of the residue and analytical aspects of dimethoate has been completed if it is determined that omethoate is a major residue.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to dimethoate, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Dimethoate was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1997) *Pesticide residues in food – 1996 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/97.1).

WHO (2003) *Dimethoate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, 1World Health Organization (WHO/SDE/WSH/03.04/90).

12.54(a) 1,4-Dioxane

1,4-Dioxane is used as a stabilizer in chlorinated solvents and as a solvent for resins, oils and waxes, for agricultural and biochemical intermediates and for adhesives, sealants, cosmetics, pharmaceuticals, rubber chemicals and surface coatings.

Guideline value	0.05 mg/litre (derived using TDI approach as well as linear multistage modelling)
Occurrence	Has been measured in surface water at concentrations up to 40 µg/litre and in groundwater at concentrations up to 80 µg/litre
TDI	16 µg/kg of body weight, based on a NOAEL of 16 mg/kg of body weight per day for hepatocellular tumours observed in a long-term drinking-water study in rats, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for non-genotoxic carcinogenicity)
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day
Basis of guideline derivation based on carcinogenicity	Linear multistage model applied to data for hepatic tumours from drinking-water studies in rats
Limit of detection	0.1–50 µg/litre by GC/MS
Treatment achievability	Not removed using conventional water treatment processes; effectively removed by biological activated carbon treatment
Additional comments	Similar guideline values were derived using the TDI approach (assuming 1,4-dioxane is not genotoxic in humans at low doses) and linear multistage modelling (because the compound clearly induces multiple tumours in various organs).

Toxicological review

1,4-Dioxane caused hepatic and nasal cavity tumours in rodents in most long-term oral studies conducted. Tumours in peritoneum, skin and mammary gland were also observed in rats given a high dose. Lung tumours were specifically detected after intraperitoneal injection. Although cohort studies of workers did not reveal any elevation in the incidence of death by cancer, a significant increase in the incidence of liver cancer was found in a comparative mortality study. However, the evidence is inadequate for human carcinogenicity assessment because of small samples or lack of

exposure data. A possibly weak genotoxic potential of 1,4-dioxane has been suggested. IARC has classified 1,4-dioxane as Group 2B (possibly carcinogenic to humans).

History of guideline development

1,4-Dioxane was not referred to in the 1958, 1963 and 1971 WHO *International Standards for Drinking-water*, the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, the second edition of the Guidelines, published in 1993, or the third edition, published in 2004.

Assessment date

The risk assessment was conducted in 2004.

Principal reference

WHO (2005) *1,4-Dioxane in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/120).

12.55 Diquat

Diquat (CAS No. 2764-72-9) is a non-selective contact herbicide and crop desiccant. Diquat may also be used (at or below 1 mg/litre) as an aquatic herbicide for the control of free-floating and submerged aquatic weeds in ponds, lakes and irrigation ditches. Because of its rapid degradation in water and strong adsorption onto sediments, diquat has rarely been found in drinking-water.

Diquat does not appear to be carcinogenic or genotoxic. The main toxicological finding in experimental animals is cataract formation. A health-based value of 6 µg/litre for diquat ion can be calculated on the basis of an ADI of 0.002 mg of diquat ion per kg of body weight, based on cataract formation at the next higher dose in a 2-year study in rats. However, because diquat has rarely been found in drinking-water, it is not considered necessary to derive a guideline value. It should also be noted that the limit of detection of diquat in water is 0.001 mg/litre, and its practical quantification limit is about 0.01 mg/litre.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to diquat, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Diquat was not evaluated in the first two editions of the *Guidelines for Drinking-water Quality*, published in 1984 and 1993. In the addendum to the second edition of these Guidelines, published in 1998, a health-based value of 0.006 mg/litre was calculated for the diquat ion using the ADI established by JMPR in 1993. However, the limit of detection of diquat in water is 0.001 mg/litre, and its practical quantification limit is about 0.01 mg/litre.

A provisional guideline value of 0.01 mg/litre was therefore established for diquation.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1994) *Pesticide residues in food – 1993. Evaluations – 1993. Part II – Toxicology.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/94.4).

WHO (2003) *Diquat in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/91).

12.56 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 will combine. The removal of EDTA from communal wastewater by biodegradation in sewage purification plants is very limited.

Guideline value	0.6 mg/litre (for EDTA as the free acid)
Occurrence	Present in surface waters generally at concentrations below 70 µg/litre, although higher concentrations (900 µg/litre) have been measured; detected in drinking-water prepared from surface waters at concentrations of 10–30 µg/litre
ADI	1.9 mg/kg of body weight as the free acid (ADI of 2.5 mg/kg of body weight proposed by JECFA for calcium disodium edetate as a food additive)
Limit of detection	1 µg/litre by potentiometric stripping analyis
Treatment achievability	0.01 mg/litre using GAC plus ozonation
Guideline derivation • allocation to water • weight • consumption	 1% of ADI 60-kg adult 2 litres/day
Additional comments	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.

Toxicological review

Calcium disodium edetate is poorly absorbed from the gut. The long-term toxicity of EDTA is complicated by its ability to chelate essential and toxic metals. Those toxicological studies that are available indicate that the apparent toxicological effects of EDTA have in fact been due to zinc deficiency as a consequence of complexation. EDTA does not appear to be teratogenic or carcinogenic in animals. The vast clinical experience of the use of EDTA in the treatment of metal poisoning has demonstrated its safety in humans.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not

refer to edetic acid. The 1993 Guidelines proposed a provisional health-based guideline value of 0.2 mg/litre for edetic acid, based on an ADI for calcium disodium edetate as a food additive proposed by JECFA in 1973 and assuming that a 10-kg child consumes 1 litre of water per day, in view of the possibility of zinc complexation. The value was considered provisional to reflect the fact that the JECFA ADI had not been considered since 1973. JECFA further evaluated the toxicological studies available on EDTA in 1993 and was unable to add any further important information regarding the toxicity of EDTA and its calcium and sodium salts to the 1973 evaluation. In the addendum to the second edition of the Guidelines, published in 1998, a guideline value of 0.6 mg/litre was derived for EDTA (free acid), using different assumptions from those used in the derivation of the provisional guideline value in the 1993 Guidelines. In particular, it was noted that the ability of EDTA to complex, and therefore reduce the availability of, zinc was of significance only at elevated doses substantially in excess of those encountered in the environment.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Edetic acid (EDTA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/58).

12.57 Endosulfan

Endosulfan (CAS No. 115-29-7) is an insecticide used in countries throughout the world to control pests on fruit, vegetables and tea and on non-food crops such as tobacco and cotton. In addition to its agricultural use, it is used in the control of the tsetse fly, as a wood preservative and for the control of home garden pests. Endosulfan contamination does not appear to be widespread in the aquatic environment, but the chemical has been found in agricultural runoff and rivers in industrialized areas where it is manufactured or formulated, as well as in surface water and groundwater samples collected from hazardous waste sites in the USA. Surface water samples in the USA generally contain less than 1 µg/litre. The main source of exposure of the general population is food, but residues have generally been found to be well below the FAO/WHO maximum residue limits. Another important route of exposure to endosulfan for the general population is the use of tobacco products.

JMPR concluded that endosulfan is not genotoxic, and no carcinogenic effects were noted in long-term studies using mice and rats. The kidney is the target organ for toxicity. Several recent studies have shown that endosulfan, alone or in combination with other pesticides, may bind to estrogen receptors and perturb the endocrine system. A

health-based value of 20 µg/litre can be calculated for endosulfan on the basis of an ADI of 0.006 mg/kg of body weight, based on results from a 2-year dietary study of toxicity in rats, and supported by a 78-week study in mice, a 1-year study in dogs and a developmental toxicity study in rats. However, because endosulfan occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to endosulfan, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Endosulfan was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1999) *Pesticide residues in food – 1998 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/99.18).

WHO (2003) *Endosulfan in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/92).

12.58 Endrin

Endrin (CAS No. 72-20-8) is a broad-spectrum foliar insecticide that acts against a wide range of agricultural pests. It is also used as a rodenticide. Small amounts of endrin are present in food, but the total intake from food appears to be decreasing.

Guideline value	0.0006 mg/litre (0.6 µg/litre)
Occurrence	Traces of endrin found in the drinking-water supplies of several countries
PTDI	0.0002 mg/kg of body weight, based on a NOAEL of 0.025 mg/kg of body weight per day in a 2-year study in dogs and applying an uncertainty factor of 100
Limit of detection	0.002 µg/litre by GC with ECD
Treatment achievability	0.2 µg/litre should be achievable using GAC

Guideline derivation	
• allocation to water	10% of PTDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	Endrin is listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines.

Toxicological review

Toxicological data are insufficient to indicate whether endrin is a carcinogenic hazard to humans. The primary site of action of endrin is the central nervous system.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to endrin, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Endrin was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1995) *Pesticide residues in food – 1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO Toxicological and Environmental Core Assessment Groups*. Rome, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 127).

IPCS (1992) *Endrin*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 130).

WHO (2003) *Endrin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/93).

12.59 Epichlorohydrin

Epichlorohydrin is used for the manufacture of glycerol, unmodified epoxy resins and water treatment resins. No quantitative data are available on its occurrence in food or drinking-water. Epichlorohydrin is hydrolysed in aqueous media.

Provisional guideline value	0.0004 mg/litre (0.4 µg/litre) The guideline value is considered to be provisional because of the uncertainties surrounding the toxicity of epichlorohydrin and the use of a large uncertainty factor in deriving the guideline value.
Occurrence	No quantitative data available
TDI	0.14 µg/kg of body weight, on the basis of a LOAEL of 2 mg/kg of body weight per day for forestomach hyperplasia observed in a 2-year gavage study in rats, correcting for 5 days per week dosing and using an uncertainty factor of 10 000 to take into consideration inter- and intraspecies variation (100), the use of a LOAEL instead of a NOAEL (10) and carcinogenicity (10)
Limit of detection	0.01 µg/litre by GC with ECD; 0.1 and 0.5 µg/litre by GC/MS; 0.01 mg/litre by GC with FID
Treatment achievability	Conventional treatment processes do not remove epichlorohydrin. Epichlorohydrin concentrations in drinking- water are controlled by limiting either the epichlorohydrin content of polyamine flocculants or the dose used, or both.
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	Although epichlorohydrin is a genotoxic carcinogen, the use of the linearized multistage model for estimating cancer risk was considered inappropriate because tumours are seen only at the site of administration, where epichlorohydrin is highly irritating.

Toxicological review

Epichlorohydrin is rapidly and extensively absorbed following oral, inhalation or dermal exposure. It binds easily to cellular components. Major toxic effects are local irritation and damage to the central nervous system. It induces squamous cell carcinomas in the nasal cavity by inhalation and forestomach tumours by the oral route. It has been shown to be genotoxic *in vitro* and *in vivo*. IARC has placed epichlorohydrin in Group 2A (probably carcinogenic to humans).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to epichlorohydrin. The 1993 Guidelines proposed a provisional health-based guideline value of 0.0004 mg/litre for epichlorohydrin. The value was provisional because it was derived using an uncertainty factor of 10 000. It was noted that a practical quantification level for epichlorohydrin is of the order of 0.03 mg/litre, but concentrations in drinking-water can be controlled by specifying the epichlorohydrin content of products coming into contact with it.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Epichlorohydrin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/94).

12.60 Ethylbenzene

The primary sources of ethylbenzene in the environment are the petroleum industry and the use of petroleum products. Because of its physical and chemical properties, more than 96% of ethylbenzene in the environment can be expected to be present in air. Values of up to 26 μg/m^3 in air have been reported. Ethylbenzene is found in trace amounts in surface water, groundwater, drinking-water and food.

Guideline value	0.3 mg/litre
Occurrence	Concentrations in drinking-water are generally below 1 μg/litre; levels up to 300 μg/litre have been reported in groundwater contaminated by point emissions.
TDI	97.1 μg/kg of body weight, based on a NOAEL of 136 mg/kg of body weight per day for hepatotoxicity and nephrotoxicity observed in a limited 6-month study in rats, correcting for 5 days per week dosing and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the limited database and short duration of the study)
Limit of detection	0.002–0.005 μg/litre by GC with photoionization detector; 0.03–0.06 μg/litre by GC/MS
Treatment achievability	0.001 mg/litre should be achievable using air stripping
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	The guideline value exceeds the lowest reported odour threshold for ethylbenzene in drinking-water (0.002 mg/litre).

Toxicological review

Ethylbenzene is readily absorbed by oral, inhalation or dermal routes. In humans, storage in fat has been reported. Ethylbenzene is almost completely converted to soluble metabolites, which are excreted rapidly in urine. The acute oral toxicity is low. No definite conclusions can be drawn from limited teratogenicity data. No data on reproduction, long-term toxicity or carcinogenicity are available. Ethylbenzene has shown no evidence of genotoxicity in *in vitro* or in *in vivo* systems.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to ethylbenzene. The 1993 Guidelines proposed a health-based guideline value of 0.3 mg/litre for ethylbenzene, noting that this value exceeds the lowest reported odour threshold for ethylbenzene in drinking-water (0.002 mg/litre).

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Ethylbenzene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/26).

12.61 Fenitrothion

Fenitrothion (CAS No. 122-14-5) is mainly used in agriculture for controlling insects on rice, cereals, fruits, vegetables, stored grains and cotton and in forest areas. It is also used for the control of flies, mosquitos and cockroaches in public health programmes and/or indoor use. Fenitrothion is stable in water only in the absence of sunlight or microbial contamination. In soil, biodegradation is the primary route of degradation, although photolysis may also play a role. Fenitrothion residues detected in water were low (maximum 1.30 µg/litre) during the spruce budworm spray programme. Following the spraying of forests to control spruce budworm, water samples did not contain detectable amounts of fenitrothion; post-spray samples contained <0.01 µg/litre. Levels of fenitrothion residues in fruits, vegetables and cereal grains decline rapidly after treatment, with a half-life of 1–2 days. Intake of fenitrothion appears to be primarily (95%) from food.

On the basis of testing in an adequate range of studies *in vitro* and *in vivo*, JMPR concluded that fenitrothion is unlikely to be genotoxic. It also concluded that fenitrothion is unlikely to pose a carcinogenic risk to humans. In long-term studies of toxicity, inhibition of cholinesterase activity was the main toxicological finding in all species. A health-based value of 8 µg/litre can be calculated for fenitrothion on the basis of an ADI of 0.005 mg/kg of body weight, based on a NOAEL of 0.5 mg/kg of body weight per day for inhibition of brain and erythrocyte cholinesterase activity in a 2-year study of toxicity in rats and supported by a NOAEL of 0.57 mg/kg of body weight per day for inhibition of brain and erythrocyte cholinesterase activity in a 3-month study of ocular toxicity in rats and a NOAEL of 0.65 mg/kg of body weight per day for reduced food consumption and body weight gain in a study of reproductive toxicity in rats, and allocating 5% of the ADI to drinking-water. However, because

fenitrothion occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to fenitrothion, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Fenitrothion was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2001) *Pesticide residues in food – 2000 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/01.3).

WHO (2003) *Fenitrothion in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/95).

12.62 Fenoprop (2,4,5-TP; 2,4,5-trichlorophenoxy propionic acid)

The half-lives for degradation of chlorophenoxy herbicides, including fenoprop (CAS No. 93-72-1), in the environment are in the order of several days. Chlorophenoxy herbicides are not often found in food.

Guideline value	0.009 mg/litre
Occurrence	Chlorophenoxy herbicides not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre
TDI	3 µg/kg of body weight, based on a NOAEL of 0.9 mg/kg of body weight for adverse effects on the liver in a study in which beagle dogs were administered fenoprop in the diet for 2 years, with an uncertainty factor of 300 (100 for inter- and intraspecies variation and 3 for limitations in the database)
Limit of detection	0.2 µg/litre by either packed or capillary column GC with ECD
Treatment achievability	No data found; 0.001 mg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, the available data from studies in exposed populations and animals do not permit assessment of the carcinogenic potential to humans of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. Effects observed in long-term studies with beagle dogs given fenoprop in the diet include mild degeneration and necrosis of hepatocytes and fibroblastic proliferation in one study and severe liver pathology in another study. In rats, increased kidney weight was observed in two long-term dietary studies.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorophenoxy herbicides, including fenoprop, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Fenoprop was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.009 mg/litre for fenoprop.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/44).

12.63 Fluoride

Fluoride accounts for about 0.3 g/kg of the Earth's crust and exists in the form of fluorides in a number of minerals. The most important source of fluoride in drinking-water is naturally occurring. Inorganic fluoride-containing minerals are used widely in industry for a wide range of purposes, including aluminium production. Fluorides can be released to the environment from the phosphate-containing rock used to produce phosphate fertilizers; these phosphate deposits contain about 4% fluorine. Fluorosilicic acid, sodium hexafluorosilicate and sodium fluoride are used in municipal water fluoridation schemes. Daily exposure to fluoride depends mainly on the geographical area. In most circumstances, food seems to be the primary source of fluoride intake, with lesser contributions from drinking-water and from toothpaste. In areas with relatively high concentrations, particularly in groundwater, drinking-water

becomes increasingly important as a source of fluoride. Intakes in areas where high-fluoride coal is used indoors may also be significant.

Guideline value	1.5 mg/litre
Occurrence	In groundwater, concentrations vary with the type of rock the water flows through but do not usually exceed 10 mg/litre; the highest natural level reported is 2800 mg/litre.
Basis of guideline derivation	Epidemiological evidence that concentrations above this value carry an increasing risk of dental fluorosis, and progressively higher concentrations lead to increasing risks of skeletal fluorosis. The value is higher than that recommended for artificial fluoridation of water supplies, which is usually 0.5–1.0 mg/litre.
Limit of detection	0.01 mg/litre by ion chromatography; 0.1 mg/litre by ion- selective electrodes or the SPADNS (sulfo phenyl azo dihydroxy naphthalene disulfonic acid) colorimetric method
Treatment achievability	1 mg/litre should be achievable using activated alumina (not a "conventional" treatment process, but relatively simple to install filters)
Additional comments	• A management guidance document on fluoride is available. • In setting national standards for fluoride or in evaluating the possible health consequences of exposure to fluoride, it is essential to consider the intake of water by the population of interest and the intake of fluoride from other sources (e.g., from food, air and dental preparations). Where the intakes from other sources are likely to approach, or be greater than, 6 mg/day, it would be appropriate to consider setting standards at a lower concentration than the guideline value. • In areas with high natural fluoride levels in drinking-water, the guideline value may be difficult to achieve, in some circumstances, with the treatment technology available.

Toxicological review

Many epidemiological studies of possible adverse effects of the long-term ingestion of fluoride via drinking-water have been carried out. These studies clearly establish that fluoride primarily produces effects on skeletal tissues (bones and teeth). In many regions with high fluoride exposure, fluoride is a significant cause of morbidity. Low concentrations provide protection against dental caries, especially in children. The pre- and post-eruptive protective effects of fluoride (involving the incorporation of fluoride into the matrix of the tooth during its formation, the development of shallower tooth grooves, which are consequently less prone to decay, and surface contact with enamel) increase with fluoride concentration up to about 2 mg/litre of drinking-water; the minimum concentration of fluoride in drinking-water required to produce it is approximately 0.5 mg/litre. However, fluoride can also have an adverse effect on tooth enamel and may give rise to mild dental fluorosis at drinking-water concentrations between 0.9 and 1.2 mg/litre, depending on intake. Elevated fluoride intakes can also have more serious effects on skeletal tissues. It has been concluded that there is

a clear excess risk of adverse skeletal effects for a total intake of 14 mg/day and suggestive evidence of an increased risk of effects on the skeleton at total fluoride intakes above about 6 mg/day.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* referred to fluoride, stating that concentrations in drinking-water in excess of 1.0–1.5 mg of fluorine per litre may give rise to dental fluorosis in some children, and much higher concentrations may eventually result in skeletal damage in both children and adults. To prevent the development of dental caries in children, a number of communal water supplies are fluoridated to bring the fluorine concentration to 1.0 mg/litre. The 1971 International Standards recommended control limits for fluorides in drinking-water for various ranges of the annual average of maximum daily air temperatures; control limits ranged from 0.6–0.8 mg/litre for temperatures of 26.3–32.6 °C to 0.9–1.7 mg/litre for temperatures of 10–12 °C. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 1.5 mg/litre was established for fluoride, as mottling of teeth has been reported very occasionally at higher levels. It was also noted that local application of the guideline value must take into account climatic conditions and higher levels of water intake. The 1993 Guidelines concluded that there was no evidence to suggest that the guideline value of 1.5 mg/litre set in 1984 needed to be revised. It was also recognized that in areas with high natural fluoride levels, the guideline value may be difficult to achieve in some circumstances with the treatment technology available. It was also emphasized that in setting national standards for fluoride, it is particularly important to consider climatic conditions, volume of water intake and intake of fluoride from other sources.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2002) *Fluorides*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 227).

WHO (2003) *Fluoride in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/96).

12.64 Formaldehyde

Formaldehyde occurs in industrial effluents and is emitted into air from plastic materials and resin glues. Formaldehyde in drinking-water results primarily from the oxidation of natural organic matter during ozonation and chlorination. Concentrations of up to 30 µg/litre have been found in ozonated drinking-water. Formaldehyde can also be found in drinking-water as a result of release from polyacetal plastic fittings.

Formaldehyde's physicochemical properties suggest that it is unlikely to volatilize from water, so exposure by inhalation during showering is expected to be low.

Rats and mice exposed to formaldehyde by inhalation exhibited an increased incidence of carcinomas of the nasal cavity at doses that caused irritation of the nasal epithelium. Ingestion of formaldehyde in drinking-water for 2 years caused stomach irritation in rats. Papillomas of the stomach associated with severe tissue irritation were observed in one study. IARC has classified formaldehyde in Group 2A (probably carcinogenic to humans). The weight of evidence indicates that formaldehyde is not carcinogenic by the oral route.

Owing to formaldehyde's high reactivity, effects in the tissue of first contact following ingestion are more likely to be related to the concentration of the formaldehyde consumed than to its total intake. A tolerable concentration of 2.6 mg/litre for ingested formaldehyde has been established based on a NOEL of 260 mg/litre for histopathological effects in the oral and gastric mucosa of rats administered formaldehyde in their drinking-water for 2 years, using an uncertainty factor of 100 (10 for interspecies variation and 10 for intraspecies variation). In view of the significant difference between the expected concentrations of formaldehyde in drinking-water and the tolerable concentration, it is not considered necessary to set a formal guideline value for formaldehyde.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to formaldehyde. The second edition of the Guidelines established a health-based guideline value of 0.9 mg/litre for formaldehyde in drinking-water. This value was brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (2002) *Formaldehyde.* Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 40).

WHO (2005) *Formaldehyde in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/48).

12.65 Glyphosate and AMPA

Glyphosate (CAS No. 1071-83-6) 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) (CAS No. 1066-51-9). 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.

Glyphosate and AMPA have similar toxicological profiles, and both are considered to exhibit low toxicity. A health-based value of 0.9 mg/litre can be derived based on the group ADI for AMPA alone or in combination with glyphosate of 0.3 mg/kg of body weight, based upon a NOAEL of 32 mg/kg of body weight per day, the highest dose tested, identified in a 26-month study of toxicity in rats fed technical-grade glyphosate and using an uncertainty factor of 100.

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

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to glyphosate, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Glyphosate was not evaluated in the first two editions of the *Guidelines for Drinking-water Quality*, published in 1984 and 1993. In the addendum to these Guidelines, published in 1998, a health-based value of 5 mg/litre was derived for glyphosate using the ADI derived in the EHC monograph for glyphosate published in 1994. However, the health-based value 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 it was not deemed necessary to establish a guideline value for glyphosate. It was noted that most AMPA, the major metabolite of glyphosate, found in water comes from sources other than glyphosate degradation.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1998) *Pesticide residues in food – 1997 evaluations. Part II – Toxicological and environmental*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/98.6).

IPCS (1994) *Glyphosate*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 159).

WHO (2003) *Glyphosate and AMPA in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/97).

12.66 Halogenated acetonitriles (dichloroacetonitrile, dibromoacetonitrile, bromochloroacetonitrile, trichloroacetonitrile)

Halogenated acetonitriles are produced during water chlorination or chloramination from naturally occurring substances, including algae, fulvic acid and proteinaceous material. In general, increasing temperature and/or decreasing pH have been associated with increasing concentrations of halogenated acetonitriles. Ambient bromide levels appear to influence, to some degree, the speciation of halogenated acetonitrile compounds. Dichloroacetonitrile is by far the most predominant halogenated acetonitrile species detected in drinking-water.

Provisional guideline value for dichloroacetonitrile	0.02 mg/litre The guideline value for dichloroacetonitrile is provisional due to limitations of the toxicological database.
Guideline value for dibromoacetonitrile	0.07 mg/litre
Occurrence	Halogenated acetonitriles have been found in surface water and groundwater distribution systems at concentrations generally below 10 µg/litre and usually below 1 µg/litre.
TDIs	
Dichloroacetonitrile	2.7 µg/kg of body weight based on a LOAEL of 8 mg/kg of body weight per day for increased relative liver weight in male and female rats in a 90-day study, using an uncertainty factor of 3000 (taking into consideration intra- and interspecies variation, the short duration of the study, the use of a minimal LOAEL and database deficiencies)
Dibromoacetonitrile	11 µg/kg of body weight, based on a NOAEL of 11.3 mg/kg of body weight per day for decreased body weight in male F344 rats in a 90-day drinking-water study and an uncertainty factor of 1000 (accounting for inter- and intraspecies variation, subchronic to chronic extrapolation and database insufficiencies)
Limit of detection	0.03 µg/litre by GC with an ECD

Treatment achievability	Concentrations of individual halogenated acetonitriles can exceed 0.01 mg/litre, although levels of 0.002 mg/litre or less are more usual. Trichloroacetonitrile concentrations are likely to be much less than 0.001 mg/litre. Reduction of organic precursors will reduce their formation.
Guideline derivation	
• allocation to water	20% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

IARC has concluded that dichloro-, dibromo-, bromochloro- and trichloroacetonitrile are not classifiable as to their carcinogenicity in humans. Dichloroacetonitrile and bromochloroacetonitrile have been shown to be mutagenic in bacterial assays, whereas results for dibromoacetonitrile and trichloroacetonitrile were negative. All four of these halogenated acetonitriles induced sister chromatid exchange and DNA strand breaks and adducts in mammalian cells *in vitro* but were negative in the mouse micronucleus test.

The majority of reproductive and developmental toxicity studies of the halogenated acetonitriles were conducted using tricaprylin as a vehicle for gavage administration of the compound under study. As tricaprylin was subsequently demonstrated to be a developmental toxicant that potentiated the effects of trichloroacetonitrile and, presumably, other halogenated acetonitriles, results reported for developmental studies using tricaprylin as the gavage vehicle are likely to overestimate the developmental toxicity of these halogenated acetonitriles.

Dichloroacetonitrile

Dichloroacetonitrile induced decreases in body weight and increases in relative liver weight in short-term studies. Although developmental toxicity has been demonstrated, the studies used tricaprylin as the vehicle for gavage administration.

Dibromoacetonitrile

Dibromoacetonitrile is currently under test for chronic toxicity in mice and rats. None of the available reproductive or developmental studies were adequate to use in the quantitative dose–response assessment. The data gap may be particularly relevant since cyanide, a metabolite of dibromoacetonitrile, induces male reproductive system toxicity, and due to uncertainty regarding the significance of the testes effects observed in the 14-day National Toxicology Program (NTP) rat study.

Bromochloroacetonitrile

Available data are insufficient to serve as a basis for derivation of a guideline value for bromochloroacetonitrile.

Trichloroacetonitrile

Available data are also insufficient to serve as a basis for derivation of a guideline value for trichloroacetonitrile. The previous provisional guideline value of 1 µg/litre was based on a developmental toxicity study in which trichloroacetonitrile was administered by gavage in tricaprylin vehicle, and a recent re-evaluation judged this study to be unreliable in light of the finding in a more recent study that tricaprylin potentiates the developmental and teratogenic effects of halogenated acetonitriles and alters the spectrum of malformations in the fetuses of treated dams.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to halogenated acetonitriles. The 1993 Guidelines established provisional health-based guideline values of 0.09 mg/litre for dichloroacetonitrile, 0.1 mg/litre for dibromoacetonitrile and 0.001 mg/litre for trichloroacetonitrile. The guideline values were designated as provisional because of the limitations of the databases (i.e., lack of long-term toxicity and carcinogenicity bioassays). Available data were insufficient to serve as a basis for derivation of a guideline value for bromochloroacetonitrile.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2000) *Disinfectants and disinfectant by-products.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2003) *Halogenated acetonitriles in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/98).

12.67 Hardness

Hardness in water is caused by dissolved calcium and, to a lesser extent, magnesium. It is usually expressed as the equivalent quantity of calcium carbonate.

Depending on pH and alkalinity, hardness above about 200 mg/litre can result in scale deposition, particularly on heating. Soft waters with a hardness of less than about 100 mg/litre have a low buffering capacity and may be more corrosive to water pipes.

A number of ecological and analytical epidemiological studies have shown a statistically significant inverse relationship between hardness of drinking-water and cardiovascular disease. There is some indication that very soft waters may have an adverse effect on mineral balance, but detailed studies were not available for evaluation.

No health-based guideline value is proposed for hardness. However, the degree of hardness in water may affect its acceptability to the consumer in terms of taste and scale deposition (see chapter 10).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to hardness. The 1971 International Standards stated that the maximum permissible level of hardness in drinking-water was 10 mEq/litre (500 mg calcium carbonate/litre), based on the acceptability of water for domestic use. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that there was no firm evidence that drinking hard water causes any adverse effects on human health and that no recommendation on the restriction of municipal water softening or on the maintenance of a minimum residual calcium or magnesium level was warranted. A guideline value of 500 mg/litre (as calcium carbonate) was established for hardness, based on taste and household use considerations. No health-based guideline value for hardness was proposed in the 1993 Guidelines, although hardness above approximately 200 mg/litre may cause scale deposition in the distribution system. Public acceptability of the degree of hardness may vary considerably from one community to another, depending on local conditions, and the taste of water with hardness in excess of 500 mg/litre is tolerated by consumers in some instances.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Hardness in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/6).

12.68 Heptachlor and heptachlor epoxide

Heptachlor (CAS No. 76-44-8) is a broad-spectrum insecticide, the use of which has been banned or restricted in many countries. At present, the major use of heptachlor is for termite control by subsurface injection into soil. Heptachlor is quite persistent in soil, where it is mainly transformed to its epoxide. Heptachlor epoxide (CAS No. 1024-57-3) is very resistant to further degradation. Heptachlor and heptachlor epoxide bind to soil particles and migrate very slowly. Heptachlor and heptachlor epoxide have been found in drinking-water at levels of nanograms per litre. Diet is considered to represent the major source of exposure to heptachlor, although intake is decreasing.

Prolonged exposure to heptachlor has been associated with damage to the liver and central nervous system toxicity. In 1991, IARC reviewed the data on heptachlor and concluded that the evidence for carcinogenicity was sufficient in animals and inadequate in humans, classifying it in Group 2B. A health-based value of 0.03 µg/litre can be calculated for heptachlor and heptachlor epoxide on the basis of a PTDI of 0.1 µg/kg of body weight, based on a NOAEL for heptachlor of 0.025 mg/kg of body weight per day from two studies in the dog, taking into consideration inadequacies of the database and allocating 1% of the PTDI to drinking-water. However, because heptachlor and heptachlor epoxide occur at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value. It should also be noted that concentrations below 0.1 µg/litre are generally not achievable using conventional treatment technology.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to heptachlor and heptachlor epoxide, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.1 µg/litre was recommended for heptachlor and heptachlor epoxide, based on the ADI recommended by JMPR. It was noted that this guideline value was less than the value that would have been calculated by applying the multistage model at a projected incremental cancer risk of 1 per 100 000 per lifetime. The 1993 Guidelines established a health-based guideline value of 0.03 µg/litre for heptachlor, based on an ADI established by JMPR in 1991 and taking into consideration the fact that the main source of exposure seems to be food.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1992) *Pesticide residues in food – 1991. Evaluations – 1991. Part II. Toxicology*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/92.52).

FAO/WHO (1995) *Pesticide residues in food – 1994. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO Toxicological and Environmental Core Assessment Groups*. Rome, Food and Agriculture Organization of the United Nations (FAO Plant Production and Protection Paper 127).

WHO (2003) *Heptachlor and heptachlor epoxide in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/99).

12.69 Hexachlorobenzene (HCB)

The major agricultural application for HCB (CAS No. 118-74-1) was as a seed dressing for crops to prevent the growth of fungi, but its use is now uncommon. At present, it appears mainly as a by-product of several chemical processes or an impurity in some pesticides. HCB is distributed throughout the environment because it is mobile and resistant to degradation. It bioaccumulates in organisms because of its physicochemical properties and its slow elimination. HCB is commonly detected at low levels in food, and it is generally present at low concentrations in ambient air. It has been detected only infrequently, and at very low concentrations (below 0.1 µg/litre), in drinking-water supplies.

IARC has evaluated the evidence for the carcinogenicity of HCB in animals and humans and assigned it to Group 2B. HCB has been shown to induce tumours in three animal species and at a variety of sites. A health-based value of 1 µg/litre can be derived for HCB by applying the linearized multistage low-dose extrapolation model to liver tumours observed in female rats in a 2-year dietary study. Using an alternative (TD_{05}) approach, a health-based guidance value of 0.16 µg/kg body weight per day can be calculated, which corresponds to a drinking-water concentration of approximately 0.05 µg/litre, if one assumes a 1% allocation of the guidance value to drinking-water.

Because the health-based values derived from both of these approaches are considerably higher than the concentrations at which HCB is detected in drinking-water (i.e., sub-nanograms per litre), when it is detected, it is not considered necessary to establish a guideline value for HCB in drinking-water. Hexachlorobenzene is listed under the Stockholm Convention on Persistent Organic Pollutants.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to HCB, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.01 µg/litre was recommended for HCB, derived from the linear multistage extrapolation model for a cancer risk of less than 1 in 100 000 for a lifetime of exposure; it was noted that the mathematical model used involved considerable uncertainty. The 1993 Guidelines calculated a guideline value of 1 µg/litre for HCB in drinking-water, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5}.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1997) *Hexachlorobenzene*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 195).

WHO (2003) *Hexachlorobenzene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/100).

12.70 Hexachlorobutadiene (HCBD)

HCBD is used as a solvent in chlorine gas production, a pesticide, an intermediate in the manufacture of rubber compounds and a lubricant. Concentrations of up to 6 µg/litre have been reported in the effluents from chemical manufacturing plants. It is also found in air and food.

Guideline value	0.0006 mg/litre (0.6 µg/litre)
Occurrence	Has been detected in surface water at concentrations of a few micrograms per litre and in drinking-water at concentrations below 0.5 µg/litre
TDI	0.2 µg/kg of body weight, based on a NOAEL of 0.2 mg/kg of body weight per day for renal toxicity in a 2-year feeding study in rats, using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for limited evidence of carcinogenicity and genotoxicity of some metabolites)
Limit of detection	0.01 µg/litre by GC/MS; 0.18 µg/litre by GC with ECD
Treatment achievability	0.001 mg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day
Additional comments	The practical quantification level for HCBD is of the order of 2 µg/litre, but concentrations in drinking-water can be controlled by specifying the HCBD content of products coming into contact with it.

Toxicological review

HCBD is easily absorbed and metabolized via conjugation with glutathione. This conjugate can be further metabolized to a nephrotoxic derivative. Kidney tumours were observed in a long-term oral study in rats. HCBD has not been shown to be carcinogenic by other routes of exposure. IARC has placed HCBD in Group 3. Positive and negative results for HCBD have been obtained in bacterial assays for point mutation; however, several metabolites have given positive results.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not

refer to HCBD. The 1993 Guidelines derived a health-based guideline value of 0.0006 mg/litre for HCBD, noting that although a practical quantification level for HCBD is of the order of 0.002 mg/litre, concentrations in drinking-water can be controlled by specifying the HCBD content of products coming into contact with it.

Assessment date

The risk assessment was conducted in in 2003.

Principal references

IPCS (1994) *Hexachlorobutadiene*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 156).

WHO (2003) *Hexachlorobutadiene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/101).

12.71 Hydrogen sulfide

Hydrogen sulfide is a gas with an offensive "rotten eggs" odour that is detectable at very low concentrations, below 0.8 $\mu g/m^3$ in air. It is formed when sulfides are hydrolysed in water. However, the level of hydrogen sulfide found in drinking-water will usually be low, because sulfides are readily oxidized in well aerated water.

The acute toxicity to humans of hydrogen sulfide following inhalation of the gas is high; eye irritation can be observed at concentrations of 15–30 mg/m^3. Although oral toxicity data are lacking, it is unlikely that a person could consume a harmful dose of hydrogen sulfide from drinking-water. Consequently, no guideline value is proposed. However, hydrogen sulfide should not be detectable in drinking-water by taste or odour (see chapter 10).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to hydrogen sulfide. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was recommended that hydrogen sulfide should not be detectable by the consumer, based on aesthetic considerations. A guideline value was not needed, since any contamination can be easily detected by the consumer. The 1993 Guidelines did not propose a health-based guideline value, as oral toxicity data are lacking; nevertheless, it is unlikely that a person could consume a harmful dose of hydrogen sulfide from drinking-water. The taste and odour thresholds of hydrogen sulfide in water are estimated to be between 0.05 and 0.1 mg/litre.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Hydrogen sulfide in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/7).

12.72 Inorganic tin

Tin is used principally in the production of coatings used in the food industry. Food, particularly canned food, therefore represents the major route of human exposure to tin. For the general population, drinking-water is not a significant source of tin, and levels in drinking-water greater than 1–2 µg/litre are exceptional. However, there is increasing use of tin in solder, which may be used in domestic plumbing, and tin has been proposed for use as a corrosion inhibitor.

Tin and inorganic tin compounds are poorly absorbed from the gastrointestinal tract, do not accumulate in tissues and are rapidly excreted, primarily in the faeces.

No increased incidence of tumours was observed in long-term carcinogenicity studies conducted in mice and rats fed stannous chloride. Tin has not been shown to be teratogenic or fetotoxic in mice, rats or hamsters. In rats, the NOAEL in a long-term feeding study was 20 mg/kg of body weight per day.

The main adverse effect on humans of excessive levels of tin in canned beverages (above 150 mg/kg) or other canned foods (above 250 m/kg) has been acute gastric irritation. There is no evidence of adverse effects in humans associated with chronic exposure to tin.

In 1989, JECFA established a PTWI of 14 mg/kg of body weight from a TDI of 2 mg/kg of body weight on the basis that the problem with tin is associated with acute gastrointestinal irritancy, the threshold for which is about 200 mg/kg in food. This was reaffirmed by JECFA in 2000. In view of its low toxicity, the presence of tin in drinking-water does not, therefore, represent a hazard to human health. For this reason, the establishment of a guideline value for inorganic tin is not deemed necessary.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to inorganic tin. The 1971 International Standards stated that tin should be controlled in drinking-water, but that insufficient information was available to enable a tentative limit to be established. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that no action was required for tin. The establishment of a guideline value for inorganic tin was not deemed necessary in the 1993 Guidelines, as, because of the low toxicity of inorganic tin, a tentative guideline value could be derived 3 orders of magnitude higher than the normal tin concentration in drinking-water. Therefore, the presence of tin in drinking-water does not represent a hazard to human health.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Inorganic tin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/115).

12.73 Iodine

Iodine occurs naturally in water in the form of iodide. Traces of iodine are produced by oxidation of iodide during water treatment. Iodine is occasionally used for water disinfection in the field or in emergency situations.

Iodine is an essential element for the synthesis of thyroid hormones. Estimates of the dietary requirement for adult humans range from 80 to 150 µg/day; in many parts of the world, there are dietary deficiencies in iodine. In 1988, JECFA set a PMTDI for iodine of 1 mg/day (17 µg/kg of body weight per day) from all sources, based primarily on data on the effects of iodide. However, recent data from studies in rats indicate that the effects of iodine in drinking-water on thyroid hormone concentrations in the blood differ from those of iodide.

Available data therefore suggest that derivation of a guideline value for iodine on the basis of information on the effects of iodide is inappropriate, and there are few relevant data on the effects of iodine. Because iodine is not recommended for long-term disinfection, lifetime exposure to iodine concentrations such as might occur from water disinfection is unlikely. For these reasons, a guideline value for iodine has not been established at this time. There is, however, a need for guidance concerning the use of iodine as a disinfectant in emergency situations and for travellers.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to iodine. The 1993 Guidelines did not establish a guideline value for iodine because available data suggest that derivation of a guideline value for iodine on the basis of information on the effects of iodide is inappropriate and there are few relevant data on the effects of iodine; also, because iodine is not recommended for long-term disinfection, lifetime exposure to iodine concentrations such as might occur from water disinfection is unlikely.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Iodine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/46).

12.74 Iron

Iron is one of the most abundant metals in the Earth's crust. It is found in natural fresh waters at levels ranging from 0.5 to 50 mg/litre. Iron may also be present in drinking-water as a result of the use of iron coagulants or the corrosion of steel and cast iron pipes during water distribution.

Iron is an essential element in human nutrition. Estimates of the minimum daily requirement for iron depend on age, sex, physiological status and iron bioavailability and range from about 10 to 50 mg/day.

As a precaution against storage in the body of excessive iron, in 1983 JECFA established a PMTDI of 0.8 mg/kg of body weight, which applies to iron from all sources except for iron oxides used as colouring agents and iron supplements taken during pregnancy and lactation or for specific clinical requirements. An allocation of 10% of this PMTDI to drinking-water gives a value of about 2 mg/litre, which does not present a hazard to health. The taste and appearance of drinking-water will usually be affected below this level (see chapter 10).

No guideline value for iron in drinking-water is proposed.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of iron greater than 1.0 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 0.3 mg/litre was established, as a compromise between iron's use in water treatment and aesthetic considerations. No health-based guideline value for iron in drinking-water was proposed in the 1993 Guidelines, but it was mentioned that a value of about 2 mg/litre can be derived from the PMTDI established in 1983 by JECFA as a precaution against storage in the body of excessive iron. Iron stains laundry and plumbing fixtures at levels above 0.3 mg/litre; there is usually no noticeable taste at iron concentrations below 0.3 mg/litre, and concentrations of 1–3 mg/litre can be acceptable for people drinking anaerobic well water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Iron in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/8).

12.75 Isoproturon

Isoproturon (CAS No. 34123-59-6) is a selective, systemic herbicide used in the control of annual grasses and broad-leaved weeds in cereals. It can be photodegraded, hydrolysed and biodegraded and persists for periods ranging from days to weeks. It is mobile in soil. There is evidence that exposure to this compound through food is low.

Guideline value	0.009 mg/litre
Occurrence	Has been detected in surface water and groundwater, usually at concentrations below 0.1 µg/litre; levels above 0.1 µg/litre have occasionally been detected in drinking-water
TDI	3 µg/kg of body weight based on a NOAEL of approximately 3 mg/kg of body weight in a 90-day study in dogs and a 2-year Feeding study in rats, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for evidence of non-genotoxic carcinogenicity in rats)
Limit of detection	10–100 ng/litre by reverse-phase HPLC followed by UV or electrochemical detection
Treatment achievability	0.1 µg/litre should be achievable using ozonation
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Isoproturon is of low acute toxicity and low to moderate toxicity following short- and long-term exposures. It does not possess significant genotoxic activity, but it causes marked enzyme induction and liver enlargement. Isoproturon caused an increase in hepatocellular tumours in male and female rats, but this was apparent only at doses that also caused liver toxicity. Isoproturon appears to be a tumour promoter rather than a complete carcinogen.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to isoproturon, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Isoproturon was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in

1984, but the 1993 Guidelines calculated a health-based guideline value of 0.009 mg/litre for isoproturon in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Isoproturon in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/37).

12.76 Lead

Lead is used principally in the production of lead-acid batteries, solder and alloys. The organolead compounds tetraethyl and tetramethyl lead have also been used extensively as antiknock and lubricating agents in petrol, although their use for these purposes in many countries is being phased out. Owing to the decreasing use of lead-containing additives in petrol and of lead-containing solder in the food processing industry, concentrations in air and food are declining, and intake from drinking-water constitutes a greater proportion of total intake. Lead is rarely present in tap water as a result of its dissolution from natural sources; rather, its presence is primarily from household plumbing systems containing lead in pipes, solder, fittings or the service connections to homes. The amount of lead dissolved from the plumbing system depends on several factors, including pH, temperature, water hardness and standing time of the water, with soft, acidic water being the most plumbosolvent.

Guideline value	0.01 mg/litre
Occurrence	Concentrations in drinking-water are generally below 5 µg/litre, although much higher concentrations (above 100 µg/litre) have been measured where lead fittings are present.
PTWI	25 µg/kg of body weight (equivalent to 3.5 µg/kg of body weight per day) for infants and children on the basis that lead is a cumulative poison and that there should be no accumulation of body burden of lead
Limit of detection	1 µg/litre by AAS
Treatment achievability	Not a raw water contaminant; treatment not applicable
Guideline derivation	
• allocation to water	50% of PTWI
• weight	5-kg infant
• consumption	0.75 litre/day

Additional comments	• As infants are considered to be the most sensitive subgroup of the population, this guideline value will also be protective for other age groups. • Lead is exceptional in that most lead in drinking-water arises from plumbing in buildings and the remedy consists principally of removing plumbing and fittings containing lead. This requires much time and money, and it is recognized that not all water will meet the guideline immediately. Meanwhile, all other practical measures to reduce total exposure to lead, including corrosion control, should be implemented.

Toxicological review

Placental transfer of lead occurs in humans as early as the 12th week of gestation and continues throughout development. Young children absorb 4–5 times as much lead as adults, and the biological half-life may be considerably longer in children than in adults. Lead is a general toxicant that accumulates in the skeleton. Infants, children up to 6 years of age and pregnant women are most susceptible to its adverse health effects. Inhibition of the activity of d-aminolaevulinic dehydratase (porphobilinogen synthase; one of the major enzymes involved in the biosynthesis of haem) in children has been observed at blood lead levels as low as 5 µg/dl, although adverse effects are not associated with its inhibition at this level. Lead also interferes with calcium metabolism, both directly and by interfering with vitamin D metabolism. These effects have been observed in children at blood lead levels ranging from 12 to 120 µg/dl, with no evidence of a threshold. Lead is toxic to both the central and peripheral nervous systems, inducing subencephalopathic neurological and behavioural effects. There is electrophysiological evidence of effects on the nervous system in children with blood lead levels well below 30 µg/dl. The balance of evidence from cross-sectional epidemiological studies indicates that there are statistically significant associations between blood lead levels of 30 µg/dl and more and intelligence quotient deficits of about four points in children. Results from prospective (longitudinal) epidemiological studies suggest that prenatal exposure to lead may have early effects on mental development that do not persist to the age of 4 years. Research on primates has supported the results of the epidemiological studies, in that significant behavioural and cognitive effects have been observed following postnatal exposure resulting in blood lead levels ranging from 11 to 33 µg/dl. Renal tumours have been induced in experimental animals exposed to high concentrations of lead compounds in the diet, and IARC has classified lead and inorganic lead compounds in Group 2B (possible human carcinogen). However, there is evidence from studies in humans that adverse neurotoxic effects other than cancer may occur at very low concentrations of lead and that a guideline value derived on this basis would also be protective for carcinogenic effects.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.1 mg/litre for lead, based on health concerns.

This value was lowered to 0.05 mg/litre in the 1963 International Standards. The tentative upper concentration limit was increased to 0.1 mg/litre in the 1971 International Standards, because this level was accepted in many countries and the water had been consumed for many years without apparent ill effects, and it was difficult to reach a lower level in countries where lead pipes were used. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.05 mg/litre was recommended. The 1993 Guidelines proposed a health-based guideline value of 0.01 mg/litre, using the PTWI established by JECFA for infants and children, on the basis that lead is a cumulative poison and that there should be no accumulation of body burden of lead. As infants are considered to be the most sensitive subgroup of the population, this guideline value would also be protective for other age groups. The Guidelines also recognized that lead is exceptional, in that most lead in drinking-water arises from plumbing, and the remedy consists principally of removing plumbing and fittings containing lead. As this requires much time and money, it is recognized that not all water will meet the guideline immediately. Meanwhile, all other practical measures to reduce total exposure to lead, including corrosion control, should be implemented. JECFA has reassessed lead and confirmed the previously derived PTWI.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Lead in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/9).

12.77 Lindane

Lindane (γ-hexachlorocyclohexane, γ-HCH) (CAS No. 58-89-9) is used as an insecticide on fruit and vegetable crops, for seed treatment and in forestry. It is also used as a therapeutic pesticide in humans and animals. Several countries have restricted the use of lindane. Lindane can be degraded in soil and rarely leaches to groundwater. In surface waters, it can be removed by evaporation. Exposure of humans occurs mainly via food, but this is decreasing. There may also be exposure from its use in public health and as a wood preservative.

Guideline value	0.002 mg/litre
Occurrence	Has been detected in both surface water and groundwater, usually at concentrations below 0.1 µg/litre, although concentrations as high as 12 µg/litre have been measured in wastewater-contaminated rivers
ADI	0.005 mg/kg of body weight on the basis of a NOAEL of 0.47 mg/kg of body weight per day in a 2-year toxicity/carcinogenicity study in rats in which an increased incidence of periacinar hepatocellular hypertrophy, increased liver and spleen weights and increased mortality occurred at higher doses, using an uncertainty factor of 100
Limit of detection	0.01 µg/litre using GC
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	1% of ADI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Lindane was toxic to the kidney and liver after administration orally, dermally or by inhalation in short-term and long-term studies of toxicity and reproductive toxicity in rats. The renal toxicity of lindane was specific to male rats and was considered not to be relevant to human risk assessment, since it is a consequence of accumulation of α_{2u}-globulin, a protein that is not found in humans. Hepatocellular hypertrophy was observed in a number of studies in mice, rats and rabbits and was reversed only partially after recovery periods of up to 6 weeks. Lindane did not induce a carcinogenic response in rats or dogs, but it caused an increased incidence of adenomas and carcinomas of the liver in agouti and pseudoagouti mice, but not in black or any other strains of mice, in a study of the role of genetic background in the latency and incidence of tumorigenesis. JMPR has concluded that there was no evidence of genotoxicity. In the absence of genotoxicity and on the basis of the weight of the evidence from the studies of carcinogenicity, JMPR has concluded that lindane is not likely to pose a carcinogenic risk to humans. Further, in an epidemiological study designed to assess the potential association between breast cancer and exposure to chlorinated pesticides, no correlation with lindane was found.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to lindane, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 3 µg/litre was recommended for lindane, based on the ADI recommended by JMPR. The 1993 Guidelines established a health-based guideline value of 2 µg/litre for lindane in drinking-water, on the basis of a study used to establish an ADI by JMPR

in 1989 but using a compound intake estimate considered to be more appropriate in light of additional data and recognizing that there may be substantial exposure to lindane from its use in public health and as a wood preservative.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2002) *Pesticide residues in food – 2002.* Rome, Food and Agriculture Organization of the United Nations, Joint FAO/WHO Meeting on Pesticide Residues (FAO Plant Production and Protection Paper 172).

WHO (2003) *Lindane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/102).

12.78 Malathion

Malathion (CAS No. 121-75-5) is commonly used to control mosquitos and a variety of insects that attack fruits, vegetables, landscaping plants and shrubs. It can also be found in other pesticide products used indoors, on pets to control ticks and insects and to control human head and body lice. Under least favourable conditions (i.e., low pH and little organic content), malathion may persist in water with a half-life of months or even years. However, under most conditions, the half-life appears to be roughly 7–14 days. Malathion has been detected in surface water and drinking-water at concentrations below 2 µg/litre.

Malathion inhibits cholinesterase activity in mice, rats and human volunteers. It increased the incidence of liver adenomas in mice when administered in the diet. Most of the evidence indicates that malathion is not genotoxic, although some studies indicate that it can produce chromosomal aberrations and sister chromatid exchange *in vitro.* JMPR has concluded that malathion is not genotoxic.

A health-based value of 0.9 mg/litre can be calculated for malathion based on an allocation of 10% of the JMPR ADI – based on a NOAEL of 29 mg/kg of body weight per day in a 2-year study of toxicity and carcinogenicity in rats, using an uncertainty factor of 100 and supported by a NOAEL of 25 mg/kg of body weight per day in a developmental toxicity study in rabbits – to drinking-water. However, intake of malathion from all sources is generally low and well below the ADI. As the chemical occurs in drinking-water at concentrations much lower than the health-based value, the presence of malathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, it is considered unnecessary to derive a guideline value for malathion in drinking-water.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to malathion, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Malathion was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1998) *Pesticide residues in food – 1997 evaluations. Part II – Toxicological and environmental*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/98.6).

WHO (2003) *Malathion in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/103).

12.79 Manganese

Manganese is one of the most abundant metals in the Earth's crust, usually occurring with iron. It is used principally in the manufacture of iron and steel alloys, as an oxidant for cleaning, bleaching and disinfection as potassium permanganate and as an ingredient in various products. More recently, it has been used in an organic compound, MMT, as an octane enhancer in petrol in North America. Manganese greensands are used in some locations for potable water treatment. Manganese is an essential element for humans and other animals and occurs naturally in many food sources. The most important oxidative states for the environment and biology are Mn^{2+}, Mn^{4+} and Mn^{7+}. Manganese is naturally occurring in many surface water and groundwater sources, particularly in anaerobic or low oxidation conditions, and this is the most important source for drinking-water. The greatest exposure to manganese is usually from food.

Guideline value	0.4 mg/litre
Occurrence	Levels in fresh water typically range from 1 to 200 µg/litre, although levels as high as 10 mg/litre in acidic groundwater have been reported; higher levels in aerobic waters usually associated with industrial pollution
TDI	0.06 mg/kg of body weight, based on the upper range value of manganese intake of 11 mg/day, identified using dietary surveys, at which there are no observed adverse effects (i.e., considered a NOAEL), using an uncertainty factor of 3 to take into consideration the possible increased bioavailability of manganese from water
Limit of detection	0.01 µg/litre by AAS; 0.05 µg/litre by ICP/MS; 0.5 µg/litre by ICP/optical emission spectroscopy; 1 µg/litre by EAAS; 10 µg/litre by FAAS
Treatment achievability	0.05 mg/litre should be achievable using oxidation and filtration
Guideline derivation • allocation to water • weight • consumption	 20% of TDI (because manganese is essential trace element) 60-kg adult 2 litres/day
Additional comments	The presence of manganese in drinking-water will be objectionable to consumers if it is deposited in water mains and causes water discoloration. Concentrations below 0.05–0.1 mg/litre are usually acceptable to consumers but may sometimes still give rise to the deposition of black deposits in water mains over an extended period; this may vary with local circumstances.

Toxicological review

Manganese is an essential element for humans and other animals. Adverse effects can result from both deficiency and overexposure. Manganese is known to cause neurological effects following inhalation exposure, particularly in occupational settings, and there have been epidemiological studies that report adverse neurological effects following extended exposure to very high levels in drinking-water. However, there are a number of significant potential confounding factors in these studies, and a number of other studies have failed to observe adverse effects following exposure through drinking-water. Animal data, especially rodent data, are not desirable for human risk assessment because the physiological requirements for manganese vary among different species. Further, rodents are of limited value in assessing the neurobehavioural effects, because the neurological effects (e.g., tremor, gait disorders) seen in primates are often preceded or accompanied by psychological symptoms (e.g., irritability, emotional lability), which are not apparent in rodents. The only primate study is of limited use in a quantitative risk assessment because only one dose group was studied in a small number of animals and the manganese content in the basal diet was not provided.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of manganese greater than 0.5 mg/litre would markedly impair the potability of

the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 0.1 mg/litre was established for manganese, based on its staining properties. The 1993 Guidelines concluded that although no single study is suitable for use in calculating a guideline value, the weight of evidence from actual daily intake and toxicity studies in laboratory animals given manganese in drinking-water supports the view that a provisional health-based guideline value of 0.5 mg/litre should be adequate to protect public health. It was also noted that concentrations below 0.1 mg/litre are usually acceptable to consumers, although this may vary with local circumstances.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1999) *Manganese and its compounds*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 12).

WHO (2003) *Manganese in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/104).

12.80 MCPA [4-(2-methyl-4-chlorophenoxy)acetic acid]

MCPA (CAS No. 94-74-6) is a chlorophenoxy post-emergence herbicide that is very soluble, is highly mobile and can leach from the soil. It is metabolized by bacteria and can be photochemically degraded. MCPA has only limited persistence in water.

Guideline value	0.002 mg/litre
Occurrence	Not frequently detected in drinking-water; has been measured in surface water and groundwater at concentrations below 0.54 and 5.5 µg/litre, respectively
TDI	0.5 µg/kg of body weight, based on a NOAEL of 0.15 mg/kg of body weight for renal and liver toxicity observed at higher dose levels in a 1-year feeding study in dogs, with an uncertainty factor of 300 (100 for inter- and intraspecies variation and 3 for inadequacies in the database)
Limit of detection	0.01 µg/litre by GC/MS and by GC with ECD
Treatment achievability	0.1 µg/litre should be achievable using GAC or ozonation
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

There are only limited and inconclusive data on the genotoxicity of MCPA. IARC evaluated MCPA in 1983 and concluded that the available data on humans and experimental animals were inadequate for an evaluation of carcinogenicity. Further evaluations by IARC on chlorophenoxy herbicides in 1986 and 1987 concluded that evidence for their carcinogenicity was limited in humans and inadequate in animals (Group 2B). Recent carcinogenicity studies on rats and mice did not indicate that MCPA was carcinogenic. No adequate epidemiological data on exposure to MCPA alone are available.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to MCPA, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. MCPA was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.002 mg/litre for MCPA in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *MCPA in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/38).

12.81 Mecoprop (MCPP; [2(2-methyl-chlorophenoxy) propionic acid])

The half-lives for degradation of chlorophenoxy herbicides, including mecoprop (CAS No. 93-65-2; 7085-19-0 racemic mixture), in the environment are in the order of several days. Chlorophenoxy herbicides are not often found in food.

Guideline value	0.01 mg/litre
Occurrence	Chlorophenoxy herbicides not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre
TDI	3.33 µg/kg of body weight, based on a NOAEL of 1 mg/kg of body weight for effects on kidney weight in 1- and 2-year studies in rats, with an uncertainty factor of 300 (100 for inter- and intraspecies variation and 3 for limitations in the database)
Limit of detection	0.01 µg/litre by GC/MS; 0.01–0.02 µg/litre by GC with ECD
Treatment achievability	0.1 µg/litre should be achievable using GAC or ozonation
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, the available data from studies in exposed populations and animals do not permit assessment of the carcinogenic potential to humans of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. Effects of dietary administration of mecoprop in short- and long-term studies include decreased relative kidney weight (rats and beagle dogs), increased relative liver weight (rats), effects on blood parameters (rats and beagle dogs) and depressed body weight gain (beagle dogs).

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorophenoxy herbicides, including mecoprop, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Mecoprop was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.01 mg/litre for mecoprop.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/44).

12.82 Mercury

Mercury is used in the electrolytic production of chlorine, in electrical appliances, in dental amalgams and as a raw material for various mercury compounds. Methylation of inorganic mercury has been shown to occur in fresh water and in seawater, although almost all mercury in uncontaminated drinking-water is thought to be in the form of Hg^{2+}. Thus, it is unlikely that there is any direct risk of the intake of organic mercury compounds, especially of alkylmercurials, as a result of the ingestion of drinking-water. However, there is a possibility that methylmercury will be converted into inorganic mercury. Food is the main source of mercury in non-occupationally exposed populations; the mean dietary intake of mercury in various countries ranges from 2 to 20 µg/day per person.

Guideline value	0.006 mg/litre for inorganic mercury
Occurrence	Mercury is present in the inorganic form in surface water and groundwater at concentrations usually below 0.5 µg/litre, although local mineral deposits may produce higher levels in groundwater.
TDI	2 µg/kg of body weight for inorganic mercury based on a NOAEL of 0.23 mg/kg of body weight per day for kidney effects in a 26-week study in rats and applying an uncertainty factor of 100 (for inter- and intraspecies variation) after adjusting for 5 days/week dosing
Limit of detection	0.05 µg/litre by cold vapour AAS; 0.6 µg/litre by ICP; 5 µg/litre by FAAS
Treatment achievability	It should be possible to achieve a concentration below 1 µg/litre by treatment of raw waters that are not grossly contaminated with mercury using methods that include coagulation/sedimentation/filtration, PAC and ion exchange.
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day
Additional comments	• A similar TDI may be obtained by applying an uncertainty factor of 1000 (an additional uncertainty factor of 10 for adjustment from a LOAEL to a NOAEL) to the LOAEL for renal effects of 1.9 mg/kg of body weight per day in a 2-year NTP study in rats. • The new guideline value applies to inorganic mercury, which is the form found in drinking-water, whereas the previous guideline value applied to total (inorganic and organic) mercury.

Toxicological review

The toxic effects of inorganic mercury compounds are seen mainly in the kidney in both humans and laboratory animals following short- and long-term exposure. In rats, effects include increased absolute and relative kidney weights, tubular necrosis, proteinuria and hypoalbuminaemia. In humans, acute oral poisoning results primarily in haemorrhagic gastritis and colitis; the ultimate damage is to the kidney. The overall weight of evidence is that mercury(II) chloride has the potential to increase

the incidence of some benign tumours at sites where tissue damage is apparent and that it possesses weak genotoxic activity but does not cause point mutations.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not mention mercury. Mercury was first mentioned in the 1971 International Standards, which gave the tentative upper concentration limit for mercury as 0.001 mg/litre (total mercury), based on health concerns. It was noted that this figure was related to levels found in natural water. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, the guideline value of 0.001 mg/litre was retained for total mercury. The 1993 Guidelines also retained the guideline value of 0.001 mg/litre for total mercury, based on the PTWI for methylmercury established by JECFA in 1972 and reaffirmed by JECFA in 1988. This value was brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (2003) *Elemental mercury and inorganic mercury compounds: human health aspects*. Geneva, World Health Organization, International Programme on Chemical Safety (Concise International Chemical Assessment Document 50).

WHO (2005) *Mercury in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/10).

12.83 Methoxychlor

Methoxychlor (CAS No. 72-43-5) is an insecticide used on vegetables, fruit, trees, fodder and farm animals. It is poorly soluble in water and highly immobile in most agricultural soils. Under normal conditions of use, methoxychlor does not seem to be of environmental concern. Daily intake from food and air is expected to be below 1 µg per person. Environmental metabolites are formed preferentially under anaerobic rather than aerobic conditions and include mainly the dechlorinated and demethylated products. There is some potential for the accumulation of the parent compound and its metabolites in surface water sediments.

Guideline value	0.02 mg/litre
Occurrence	Detected occasionally in drinking-water, at concentrations as high as 300 µg/litre in rural areas
TDI	5 µg/kg of body weight, based on a systemic NOAEL of 5 mg/kg of body weight in a teratology study in rabbits, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 reflecting concern for threshold carcinogenicity and the limited database)

Limit of detection	0.001–0.01 µg/litre by GC
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

The genotoxic potential of methoxychlor appears to be negligible. In 1979, IARC assigned methoxychlor to Group 3. Subsequent data suggest a carcinogenic potential of methoxychlor for liver and testes in mice. This may be due to the hormonal activity of proestrogenic mammalian metabolites of methoxychlor and may therefore have

a threshold. The study, however, was inadequate because only one dose was used and because this dose may have been above the maximum tolerated dose. The database for studies on long-term, short-term and reproductive toxicity is inadequate. A teratology study in rabbits reported a systemic NOAEL of 5 mg/kg of body weight per day, which is lower than the LOAELs and NOAELs from other studies. This NOAEL was therefore selected for use in the derivation of a TDI.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to methoxychlor, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.03 mg/litre was recommended for methoxychlor, based on the ADI recommended by JMPR in 1965 and reaffirmed in 1977. The 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for methoxychlor in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Methoxychlor in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/105).

12.84 Methyl parathion

Methyl parathion (CAS No. 298-00-0) is a non-systemic insecticide and acaricide that is produced throughout the world and has been registered for use on many crops, in particular cotton. It partitions mainly to air and soil in the environment. There is virtually no movement through soil, and neither the parent compound nor its breakdown products will reach groundwater. By far the most important route for the environmental degradation of methyl parathion is microbial degradation. Half-lives of methyl parathion in water are in the order of weeks to months. Concentrations of methyl parathion in natural waters of agricultural areas in the USA ranged up to 0.46 µg/litre, with highest levels in summer. The general population can come into contact with methyl parathion via air, water or food.

A NOAEL of 0.3 mg/kg of body weight per day was derived from the combined results of several studies conducted in humans, based on the depression of erythrocyte and plasma cholinesterase activities. Methyl parathion decreased cholinesterase activities in long-term studies in mice and rats, but did not induce carcinogenic

effects. Methyl parathion was mutagenic in bacteria, but there was no evidence of genotoxicity in a limited range of studies in mammalian systems.

A health-based value of 9 µg/litre can be calculated for methyl parathion on the basis of an ADI of 0.003 mg/kg of body weight, based on a NOAEL of 0.25 mg/kg of body weight per day in a 2-year study in rats for retinal degeneration, sciatic nerve demyelination, reduced body weight, anaemia and decreased brain acetylcholinesterase activity, using an uncertainty factor of 100. Since the toxicological end-points seen in animals were other than acetylcholinesterase inhibition, it was considered more appropriate to use these data rather than the NOAEL derived for cholinesterase inhibition in humans.

Intake of methyl parathion from all sources is generally low and well below the ADI. As the health-based value is much higher than methyl parathion concentrations likely to be found in drinking-water, the presence of methyl parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a guideline value for methyl parathion is not deemed necessary.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to methyl parathion, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Methyl parathion was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1996) *Pesticide residues in food – 1995 evaluations. Part II – Toxicological and environmental.* Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/96.48).

IPCS (1992) *Methyl parathion*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 145).

WHO (2003) *Methyl parathion in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/106).

12.84(a) Methyl *tertiary*-butyl ether (MTBE)

The major use of MTBE is as a gasoline additive. Surface water can be contaminated by gasoline spills; however, due to the high volatility of MTBE, most is lost to evapo-

ration. Spills and leaking storage tanks can cause more serious problems in groundwater, where MTBE is more persistent. MTBE has been detected in groundwater and drinking-water at concentrations in the ng/litre to µg/litre range.

No human cancer studies have been published for either the general population or occupationally exposed cohorts. There have been a number of human studies of neurological and clinical effects of exposure to MTBE by inhalation, with mixed results. In general, no objective changes could be seen at levels of MTBE normally found, even in such microenvironments as gasoline filling stations.

The weight of evidence suggests that MTBE is not genotoxic. A large number of studies using *in vitro* and *in vivo* mammalian and non-mammalian systems have been conducted to assess the mutagenicity of MTBE, almost all of which have produced negative results. These results suggest that the mechanism of action of MTBE is more likely to be non-genotoxic than genotoxic, although no one mechanism appears to explain all of the observed effects.

It has been concluded that MTBE should be considered a rodent carcinogen but that it is not genotoxic, and the carcinogenic response is evident only at high levels of exposure that also induce other adverse effects. The available data are therefore considered inconclusive and prohibit their use for human carcinogenic risk assessment. A health-based guideline value has not been derived for MTBE, due to the fact that any guideline value that would be derived would be significantly higher than the concentration at which it would be detected by odour (15 µg/litre is the lowest level eliciting a response in a study using taste- and odour-sensitive participants).

History of guideline development

MTBE was not evaluated in WHO *International Standards for Drinking-water* or in the first, second or third editions of the *Guidelines for Drinking-water Quality*.

Assessment date

The risk assessment was conducted in 2004.

Principal references

IPCS (1998) *Methyl tertiary-butyl ether*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 206).

WHO (2005) *Methyl tertiary-butyl ether (MTBE) in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/122).

12.85 Metolachlor

Metolachlor (CAS No. 51218-45-2) is a selective pre-emergence herbicide used on a number of crops. It can be lost from the soil through biodegradation, photodegrada-

tion and volatilization. It is fairly mobile and under certain conditions can contaminate groundwater, but it is mostly found in surface water.

Guideline value	0.01 mg/litre
Occurrence	Detected in surface water and groundwater at concentrations that can exceed 10 µg/litre
TDI	3.5 µg/kg of body weight, based on a NOAEL of 3.5 mg/kg of body weight for an apparent decrease in kidney weight at the two highest dose levels in a 1-year dog study, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 reflecting some concern regarding carcinogenicity)
Limit of detection	0.75–0.01 µg/litre by GC with nitrogen–phosphorus detection
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

In a 1-year study in beagle dogs, administration of metolachlor resulted in decreased kidney weight at the two highest dose levels. In 2-year studies with rodents fed metolachlor in the diet, the only toxicological effects observed in albino mice were decreased body weight gain and decreased survival in females at the highest dose level, whereas rats showed decreased body weight gain and food consumption at the highest dose level. There is no evidence from available studies that metolachlor is carcinogenic in mice. In rats, an increase in liver tumours in females as well as a few nasal tumours in males have been observed. Metolachlor is not genotoxic.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to metolachlor, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Metolachlor was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.01 mg/litre for metolachlor in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Metolachlor in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/39).

12.86 Microcystin-LR

Among the more than 80 microcystins identified to date, only a few occur frequently and in high concentrations. Microcystin-LR is among the most frequent and most toxic microcystin congeners. Frequently occurring cyanobacterial genera that contain these toxins are *Microcystis*, *Planktothrix* and *Anabaena*. Microcystins usually occur within the cells; substantial amounts are released to the surrounding water only in situations of cell rupture (i.e., lysis).

Provisional guideline value	0.001 mg/litre (for total microcystin-LR, free plus cell-bound) The guideline value is provisional, as it covers only microcystin-LR, the database is limited and new data for the toxicity of cyanobacterial toxins are being generated.
TDI	0.04 µg/kg of body weight, based on liver pathology observed in a 13-week study in mice and applying an uncertainty factor of 1000, taking into consideration limitations in the database, in particular lack of data on chronic toxicity and carcinogenicity
Limit of detection	0.1–1 µg/litre by HPLC following extraction of cells with 75% aqueous methanol or following concentration of microcystins from liquid samples on C-18; will allow differentiation between variants where standards are available. 0.1–0.5 µg/litre by commercially available immunoassay kits (ELISA) for microcystins dissolved in water or in aqueous extracts of cells; will detect most microcystins. These are less precise in quantification than HPLC, but useful for screening. 0.5–1.5 µg/litre by protein phosphatase assay for microcystins dissolved in water or in aqueous extracts of cells; will detect all microcystins. This assay is less precise in quantification and identification than HPLC, but useful for screening.
Monitoring	The preferred approach is visual monitoring (including microscopy for potentially microcystin-containing genera) of source water for evidence of increasing cyanobacterial cell density (blooms) or bloom-forming potential, and increased vigilance where such events occur. Chemical monitoring of microcystins is not the preferred focus.
Prevention and treatment	Actions to decrease the probability of bloom occurrence include catchment and source water management, such as reducing nutrient loading or changing reservoir stratification and mixing. Treatment effective for the removal of cyanobacteria includes filtration to remove intact cells. Treatment effective against free microcystins in water (as well as most other free cyanotoxins) includes oxidation through ozone or chlorine at sufficient concentrations and contact times, as well as GAC and some PAC applications.

Guideline derivation	
• allocation to water	80% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	While guideline values are derived where sufficient data exist, they are intended to inform the interpretation of monitoring data and not to indicate that there is a requirement for routine monitoring by chemical analysis.

Toxicological review

Microcystin-LR is a potent inhibitor of eukaryotic protein serine/threonine phosphatases 1 and 2A. The primary target for microcystin toxicity is the liver, as microcystins cross cell membranes chiefly through the bile acid transporter. Guideline derivation was based on an oral 13-week study with mice, supported by an oral 44-day study with pigs. A large number of poisonings of livestock and wildlife have been recorded. Evidence of tumour promotion has been published.

History of guideline development

Cyanobacterial toxins were not evaluated in the 1958, 1963 and 1971 WHO *International Standards for Drinking-water* or in the first two editions of the *Guidelines for Drinking-water Quality*, published in 1984 and 1993. In the addendum to the second edition of the Guidelines, published in 1998, it was concluded that there were insufficient data to allow a guideline value to be derived for any cyanobacterial toxins other than microcystin-LR. A health-based guideline value for total microcystin-LR (free plus cell-bound) of 0.001 mg/litre was derived, assuming significant exposure from drinking-water. The guideline value was designated as provisional, as it covers only microcystin-LR, the database is limited and new data for the toxicity of cyanobacterial toxins are being generated.

Assessment date

The risk assessment was conducted in 2003.

Principal references

Chorus I, Bartram J, eds. (1999) *Toxic cyanobacteria in water: A guide to their public health consequences, monitoring and management.* Published by E & FN Spon, London, on behalf of the World Health Organization, Geneva.

WHO (2003) *Cyanobacterial toxins: Microcystin-LR in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/57).

12.87 Molinate

Molinate (CAS No. 2212-67-1) is a herbicide used to control broad-leaved and grassy weeds in rice. The available data suggest that groundwater pollution by molinate is

restricted to some rice-growing regions. Data on the occurrence of molinate in the environment are limited. Molinate is of low persistence in water and soil, with a half-life of about 5 days.

Guideline value	0.006 mg/litre
Occurrence	Concentrations in water rarely exceed 1 µg/litre.
TDI	2 µg/kg of body weight, based on a NOAEL for reproductive toxicity in the rat of 0.2 mg/kg of body weight, with an uncertainty factor of 100 (for inter- and intraspecies variation)
Limit of detection	0.01 µg/litre by GC/MS
Treatment achievability	0.001 mg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

On the basis of the limited information available, molinate does not seem to be carcinogenic or mutagenic in animals. Evidence suggests that impairment of the reproductive performance of the male rat represents the most sensitive indicator of molinate exposure. However, epidemiological data based on the examination of workers involved in molinate production do not indicate any effect on human fertility.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to molinate, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Molinate was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.006 mg/litre for molinate in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Molinate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/40).

12.88 Molybdenum

Molybdenum is found naturally in soil and is used in the manufacture of special steels and in the production of tungsten and pigments, and molybdenum compounds are used as lubricant additives and in agriculture to prevent molybdenum deficiency in crops.

Guideline value	0.07 mg/litre
Occurrence	Concentrations in drinking-water are usually less than 0.01 mg/litre, although concentrations as high as 200 µg/litre have been reported in areas near mining sites.
NOAEL	0.2 mg/litre in a 2-year study of humans exposed through their drinking-water, using an uncertainty factor of 3 for intraspecies variation (because molybdenum is an essential element)
Limit of detection	0.25 µg/litre by graphite furnace AAS; 2 µg/litre by ICP/AES
Treatment achievability	Molybdenum is not removed from drinking-water.
Additional comments	The guideline value is within the range of that derived on the basis of results of toxicological studies in animal species and is consistent with the essential daily requirement.

Toxicological review

Molybdenum is considered to be an essential element, with an estimated daily requirement of 0.1–0.3 mg for adults. No data are available on the carcinogenicity of molybdenum by the oral route. Additional toxicological information is needed on the impact of molybdenum on bottle-fed infants.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to molybdenum. The 1971 International Standards stated that molybdenum should be controlled in drinking-water, but that insufficient information was available to enable a tentative limit to be established. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that no action was required for molybdenum. The 1993 Guidelines proposed a health-based guideline value of 0.07 mg/litre for molybdenum based on a 2-year study of humans exposed through their drinking-water. This value is within the range of that derived on the basis of results of toxicological studies in animal species and is consistent with the essential daily requirement.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Molybdenum in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/11).

12.89 Monochloramine

Mono-, di- and trichloramines are considered by-products of drinking-water chlorination, being formed when ammonia is added to chlorinated water. Monochloramine may also be added to maintain residual disinfection activity in potable water distribution systems. The use of chloramines for disinfection instead of chlorine reduces the formation of THMs in drinking-water supplies. However, formation of other by-products, such as haloketones, chloropicrin, cyanogen chloride, haloacetic acids, haloacetonitriles, aldehydes and chlorophenols, has been reported. Monochloramine is recognized as a less effective disinfectant than chlorine. Only monochloramine, the most abundant chloramine, is considered here, as it has been the most extensively studied.

Guideline value	3 mg/litre
Occurrence	Typical chloramine concentrations of 0.5–2 mg/litre are found in drinking-water supplies where chloramine is used as a primary disinfectant or to provide a chlorine residual in the distribution system.
TDI	94 µg/kg of body weight, based on a NOAEL of 9.4 mg/kg of body weight per day, the highest dose administered to male rats in a 2-year NTP drinking-water study (although mean body weights of rats given the highest dose were lower than those of their respective control groups, it is probable that the lower body weights were caused by the unpalatability of the drinking-water)
Limit of detection	10 µg/litre by colorimetric methods
Treatment achievability	It is possible to reduce the concentration of chloramine effectively to zero (<0.1 mg/litre) by reduction; however, it is normal practice to supply water with a chloramine residual of a few tenths of a milligram per litre to act as a preservative during distribution.
Guideline derivation	
• allocation to water	100% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	• An additional uncertainty factor for possible carcinogenicity was not applied because equivocal cancer effects reported in the NTP study in only one species and in only one sex were within the range observed in historical controls. • Most individuals are able to taste chloramines at concentrations below 5 mg/litre, and some at levels as low as 0.3 mg/litre.

Toxicological review

Although monochloramine has been shown to be mutagenic in some *in vitro* studies, it has not been found to be genotoxic *in vivo*. IARC has classified chloramine in Group 3, and the US EPA has classified monochloramine in group D (not classifiable as to human carcinogenicity, as there is inadequate human and animal evidence). In the NTP bioassay in two species, the incidence of mononuclear cell leukaemias in female F344/N rats was increased, but no other increases in tumour incidence were observed. IPCS (2000) did not consider that the increase in mononuclear cell leukaemia was treatment-related.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to chloramines. The 1993 Guidelines established a health-based guideline value of 3 mg/litre for monochloramine in drinking-water. Available data were insufficient for the establishment of guideline values for dichloramine and trichloramine. It was noted that the odour thresholds for dichloramine and trichloramine are much lower than that for monochloramine.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2000) *Disinfectants and disinfectant by-products.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2003) *Monochloramine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/83).

12.90 Monochloroacetic acid

Chlorinated acetic acids are formed from organic material during water chlorination.

Guideline value	0.02 mg/litre
Occurrence	Present in surface water-derived drinking-water at <2–82 µg/litre (mean 2.1 µg/litre)
TDI	3.5 µg/kg of body weight, based on a LOAEL of 3.5 mg/kg of body weight per day from a study in which increased absolute and relative spleen weights were observed in male rats exposed to monochloroacetic acid in drinking-water for 2 years, and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for use of a minimal LOAEL instead of a NOAEL and database deficiencies, including the lack of a multigeneration reproductive toxicity study)
Limit of detection	2 µg/litre by GC with ECD; 5 µg/litre by GC/MS
Treatment achievability	No information available
Guideline derivation	
• allocation to water	20% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

No evidence of carcinogenicity of monochloroacetate was found in 2-year gavage bioassays with rats and mice. Monochloroacetate has given mixed results in a limited number of mutagenicity assays and has been negative for clastogenicity in genotoxicity studies. IARC has not classified the carcinogenicity of monochloroacetic acid.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to monochloroacetic acid. The 1993 Guidelines did not establish a guideline value for monochloroacetic acid, as available toxicity data were considered insufficient.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Monochloroacetic acid in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/85).

12.91 Monochlorobenzene

Releases of monochlorobenzene (MCB) to the environment are thought to be mainly due to volatilization losses associated with its use as a solvent in pesticide formulations, as a degreasing agent and from other industrial applications. MCB has been

detected in surface water, groundwater and drinking-water; mean concentrations were less than 1 µg/litre in some potable water sources (maximum 5 µg/litre) in Canada. The major source of human exposure is probably air.

MCB is of low acute toxicity. Oral exposure to high doses of MCB affects mainly the liver, kidneys and haematopoietic system. There is limited evidence of carcinogenicity in male rats, with high doses increasing the occurrence of neoplastic nodules in the liver. The majority of evidence suggests that MCB is not mutagenic; although it binds to DNA *in vivo*, the level of binding is low.

A health-based value of 300 µg/litre can be calculated for MCB on the basis of a TDI of 85.7 µg/kg of body weight, based on neoplastic nodules identified in a 2-year rat study with dosing by gavage, and taking into consideration the limited evidence of carcinogenicity. However, because MCB occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value. It should also be noted that the health-based value far exceeds the lowest reported taste and odour threshold for MCB in water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to MCB. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value for chlorobenzene was recommended after a detailed evaluation of the compound. Following consideration of the calculated toxicological limit for drinking-water of 0.005–0.05 mg/litre based on a tentative ADI and the fact that the threshold odour concentration of MCB in water is 0.03 mg/litre, no guideline value was recommended, and 0.003 mg/litre was recommended to avoid taste and odour problems in drinking-water. The 1993 Guidelines proposed a health-based guideline value of 0.3 mg/litre for MCB, noting that this value far exceeds the lowest reported taste and odour threshold for MCB in water (0.01 mg/litre).

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Monochlorobenzene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/107).

12.92 MX

MX, which is the common name for 3-chloro-4-dichloromethyl-5-hydroxy-2(5H)-furanone, is formed by the reaction of chlorine with complex organic matter in drinking-water. It has been identified in chlorinated humic acid solutions and drinking-water in Finland, the United Kingdom and the USA and was found to be

present in 37 water sources at levels of 2–67 ng/litre. Five drinking-water samples from different Japanese cities contained MX at concentrations ranging from <3 to 9 ng/litre.

MX is a potent mutagen in bacteria and in cells *in vitro* and has undergone a lifetime study in rats in which some tumorigenic responses were observed. These data indicate that MX induces thyroid and bile duct tumours. IARC has classified MX in Group 2B on the basis of rat tumorigenicity and its strong mutagenicity.

A health-based value of 1.8 µg/litre can be calculated for MX on the basis of the increase in cholangiomas and cholangiocarcinomas in female rats using the linearized multistage model (without a body surface area correction). However, this is significantly above the concentrations that would be found in drinking-water, and, in view of the analytical difficulties in measuring this compound at such low concentrations, it is considered unnecessary to propose a formal guideline value for MX in drinking-water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to MX. The 1993 Guidelines concluded that available data were inadequate to permit a guideline value for MX to be established.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2000) *Disinfectants and disinfectant by-products.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 216).

WHO (2003) *MX in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/108).

12.93 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, where there are areas in which nickel that naturally occurs in groundwater is mobilized or where there is use of certain types of kettles, of non-resistant material in wells or of water that has come into contact with nickel- or chromium-plated taps, the nickel contribution from water may be significant.

Guideline value	0.07 mg/litre
Occurrence	The concentration of nickel in drinking-water is normally less than 0.02 mg/litre, although nickel released from taps and fittings may contribute up to 1 mg/litre. In special cases of release from natural or industrial nickel deposits in the ground, the nickel concentrations in drinking-water may be higher.
TDI	12 µg/kg of body weight, derived from a LOAEL established after oral provocation of fasted patients with an empty stomach
Limit of detection	0.1 µg/litre by ICP-MS; 0.5 µg/litre by FAAS; 10 µg/litre by ICP-AES
Treatment achievability	20 µg/litre should be achievable by conventional treatment, e.g., coagulation. Where naturally occurring nickel is mobilized in groundwater, removal is by ion exchange or adsorption. Where nickel leaches from alloys in contact with drinking-water or from chromium- or nickel-plated taps, control is by appropriate control of materials in contact with the drinking-water and flushing taps before using the water.
Guideline derivation • allocation to water • weight • consumption	 20% of TDI 60-kg adult 2 litres/day
Additional comments	• Although the guideline value is close to the acute LOAEL, the LOAEL is based on total exposure from drinking-water, and absorption from drinking-water on an empty stomach is 10- to 40-fold higher than absorption from food. Deriving the total acceptable intake for oral challenge from studies using drinking-water on an empty stomach in fasted patients can, therefore, be considered a worst-case scenario. • A general toxicity value of 130 µg/litre could be determined from a well conducted two-generation study in rats. However, this general toxicity value may not be sufficiently protective of individuals sensitized to nickel, for whom a sufficiently high oral challenge has been shown to elicit an eczematous reaction.

Toxicological review

IARC concluded that inhaled nickel compounds are carcinogenic to humans (Group 1) and that metallic nickel is possibly carcinogenic (Group 2B). However, there is a lack of evidence of a carcinogenic risk from oral exposure to nickel. In a well conducted two-generation reproductive study in rats administered nickel by gavage, a clear NOEL was observed for adult rats and their offspring for all the end-points studied, including integrity and performance of male and female reproductive systems, growth and development of offspring and post-implantation/perinatal lethality. Allergic contact dermatitis is the most prevalent effect of nickel in the general population.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to nickel. In the first edition of the *Guidelines for Drinking-water Quality*, pub-

lished in 1984, it was concluded that the toxicological data available indicate that a guideline value for nickel in drinking-water was not required. A health-based guideline value of 0.02 mg/litre was derived in the second edition of the Guidelines, published in 1993, which should provide sufficient protection for individuals who are sensitive to nickel. This guideline value was maintained in the addendum to the second edition, published in 1998, because, on the basis of the available data, it was considered to provide sufficient protection for individuals who are sensitive to nickel. However, the guideline value was designated as provisional owing to uncertainties about the effect level for perinatal mortality. This value was brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal reference

WHO (2005) *Nickel in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/55).

12.94 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 leaching or runoff from agricultural land or contamination from human or animal wastes as a consequence of the oxidation of ammonia and similar sources. Anaerobic conditions may result in the formation and persistence of nitrite. Chloramination may give rise to the formation of nitrite within the distribution system if the formation of chloramine is not sufficiently controlled. The formation of nitrite is as a consequence of microbial activity and may be intermittent. Nitrification in distribution systems can increase nitrite levels, usually by 0.2–1.5 mg/litre.

Guideline value for nitrate	50 mg/litre to protect against methaemoglobinaemia in bottle-fed infants (short-term exposure)
Guideline value / Provisional guideline value for nitrite	• 3 mg/litre for methaemoglobinaemia in infants (short-term exposure) • 0.2 mg/litre (provisional) (long-term exposure) The guideline value for chronic effects of nitrite is considered provisional owing to uncertainty surrounding the relevance of the observed adverse health effects for humans and the susceptibility of humans compared with animals. The occurrence of nitrite in distribution as a consequence of chloramine use will be intermittent, and average exposures over time should not exceed the provisional guideline value.

Guideline value for	The sum of the ratios of the concentrations of each to its guideline
combined nitrate plus nitrite	value should not exceed 1.
Occurrence	In most countries, nitrate levels in drinking-water derived from surface water do not exceed 10 mg/litre, although nitrate levels in well water often exceed 50 mg/litre; nitrite levels are normally lower, less than a few milligrams per litre.

Basis of guideline derivation	• nitrate (bottle-fed infants): in epidemiological studies, methaemoglobinaemia was not reported in infants in areas where drinking-water consistently contained less than 50 mg of nitrate per litre • nitrite (bottle-fed infants): nitrite is 10 times more potent than nitrate on a molar basis with respect to methaemoglobin formation • nitrite (long-term exposure): based on allocation to drinking- water of 10% of JECFA ADI of 0.06 mg/kg of body weight per day, based on nitrite-induced morphological changes in the adrenals, heart and lungs in laboratory animal studies
Limit of detection	0.1 mg/litre (nitrate) and 0.05 mg/litre (nitrite) by liquid chromatography; 0.01–1 mg/litre (nitrate) by spectrometric techniques; 0.005–0.01 mg/litre (nitrite) by a molecular absorption spectrometric method; 22 µg/litre (nitrate) and 35 µg/litre (nitrite) by ion chromatography
Treatment achievability	• nitrate: 5 mg/litre or lower should be achievable using biological denitrification (surface waters) or ion exchange (groundwaters) • nitrite: 0.1 mg/litre should be achievable using chlorination (to form nitrate)
Additional comments	• Nitrite can occur in distribution at higher concentrations when chloramination is used, but the occurrence is almost invariably sporadic. Methaemoglobinaemia is therefore the most important consideration, and the guideline derived for protection against methaemoglobinaemia would be the most appropriate under these circumstances, allowing for any nitrate that may also be present. • 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. • Methaemoglobinaemia in infants also appears to be associated with simultaneous exposure to microbial contaminants.

Toxicological review

The primary health concern regarding nitrate and nitrite is the formation of methaemoglobinaemia, so-called "blue-baby syndrome." Nitrate is reduced to nitrite in the stomach of infants, and nitrite is able to oxidize haemoglobin (Hb) to methaemoglobin (metHb), which is unable to transport oxygen around the body. 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 infants under 3 months of age is less than 3%.

The Hb of young infants is more susceptible to metHb 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 metHb, still present in the blood of infants. In addition, there is a deficiency in infants of metHb reductase, the enzyme responsible for the reduction of metHb to Hb. The reduction of nitrate to nitrite by gastric bacteria is also higher in infants because of low gastric acidity. The level of nitrate in breast milk is relatively low; when bottle-fed, however, these young infants are at risk because of the potential for exposure to nitrate/nitrite in drinking-water and the relatively high intake of water in relation to body weight. The higher reduction of nitrate to nitrite in young infants is not very well quantified, but it appears that gastrointestinal infections exacerbate the conversion from nitrate to nitrite.

The weight of evidence is strongly against there being an association between nitrite and nitrate exposure in humans and the risk of cancer.

Studies with nitrite in laboratory rats have reported hypertrophy of the adrenal zona glomerulosa. The mechanism of induction of this effect and whether it occurs in other species is unclear. JECFA developed an ADI of 5 mg of potassium nitrite per kg of body weight based on the NOAEL in these studies.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* referred to nitrates, stating that the ingestion of water containing nitrates in excess of 50–100 mg/litre (as nitrate) may give rise to methaemoglobinaemia in infants under 1 year of age. In the 1963 International Standards, this value was lowered to 45 mg/litre (as nitrate), which was retained in the 1971 International Standards. The 1971 International Standards first mentioned concern over the possibility of nitrosamine formation *in vivo*; as nitrosamines are a possible hazard to human health, the 1971 Standards stated that it may eventually become necessary to reduce the level of nitrates in water if it is found that this source makes a significant contribution to the hazard to human health arising from nitrosamines. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 10 mg/litre for nitrate-nitrogen was recommended. It was also recommended that the guideline value for nitrite must be correspondingly lower than that for nitrate, and it was noted that the nitrite-nitrogen level should be considerably lower than 1 mg/litre where drinking-water is correctly treated. The 1993 Guidelines concluded that extensive epidemiological data support the current guideline value for nitrate-nitrogen of 10 mg/litre, but stated that this value should be expressed not on the basis of nitrate-nitrogen but on the basis of nitrate itself, which is the chemical entity of concern to health. The guideline value for nitrate is therefore 50 mg/litre. This guideline value for methaemoglobinaemia in infants, an acute effect, was confirmed in the addendum to the Guidelines, published in 1998. It was also concluded in the 1993 Guidelines that a guideline value for nitrite should be proposed, although no suitable animal studies of methaemoglobinaemia were available. A provisional guideline value for nitrite of 3 mg/litre was therefore proposed by accepting a relative potency for nitrite and nitrate with respect to methaemoglobin formation of 10 : 1 (on a molar basis). In the addendum to the Guidelines, published

in 1998, it was concluded that human data on nitrite reviewed by JECFA supported the current provisional guideline value of 3 mg/litre, based on induction of methaemoglobinaemia in infants. In addition, a guideline value of 0.2 mg/litre for nitrate ion associated with long-term exposure was derived in the addendum to the Guidelines, based on JECFA's ADI derived in 1995. However, because of the uncertainty surrounding the relevance of the observed adverse health effects for humans and the susceptibility of humans compared with animals, this guideline value was considered provisional. Because of the possibility of simultaneous occurrence of nitrite and nitrate in drinking-water, it was recommended in the 1993 and 1998 Guidelines that the sum of the ratios of the concentration of each to its guideline value should not exceed 1.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Nitrate and nitrite in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/56).

12.95 Nitrilotriacetic acid (NTA)

Nitrilotriacetic acid (NTA) is used primarily in laundry detergents as a replacement for phosphates and in the treatment of boiler water to prevent accumulation of mineral scale.

Guideline value	0.2 mg/litre
Occurrence	Concentrations in drinking-water usually do not exceed a few micrograms per litre, although concentrations as high as 35 µg/litre have been measured.
TDI	10 µg/kg of body weight, based on nephritis and nephrosis in a 2-year study in rats and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for carcinogenic potential at high doses)
Limit of detection	0.2 µg/litre using GC with a nitrogen-specific detector
Treatment achievability	No data available
Guideline derivation	
• allocation to water	50% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

NTA is not metabolized in animals and is rapidly eliminated, although some may be briefly retained in bone. It is of low acute toxicity to animals, but it has been shown to produce kidney tumours in rodents following long-term exposure to doses higher than those required to produce nephrotoxicity. IARC has placed NTA in Group 2B. It is not genotoxic, and the reported induction of tumours is believed to be due to cytotoxicity resulting from the chelation of divalent cations such as zinc and calcium in the urinary tract, leading to the development of hyperplasia and subsequently neoplasia.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to NTA. The 1971 International Standards stated that NTA should be controlled in drinking-water, but that insufficient information was available to enable a tentative limit to be established. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was determined that no further action on NTA was required. A health-based guideline value of 0.2 mg/litre was established for NTA in the 1993 Guidelines.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Nitrilotriacetic acid in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/30).

12.96 Parathion

Parathion (CAS No. 56-38-2) is a non-systemic insecticide that is used in many countries throughout the world. It is used as a fumigant and acaricide and as a pre-harvest soil and foliage treatment on a wide variety of crops, both outdoors and in greenhouses. Parathion released to the environment will adsorb strongly to the top layer of soil and is not likely to leach significantly. Parathion disappears from surface waters in about a week. The general population is not usually exposed to parathion from air or water. Parathion residues in food are the main source of exposure.

Parathion inhibits cholinesterase activity in all species tested. There has been no evidence of carcinogenicity in 2-year rat studies. JMPR concluded that parathion is not genotoxic.

A health-based value of 10 µg/litre can be calculated for parathion on the basis of an ADI of 0.004 mg/kg of body weight based on a NOAEL of 0.4 mg/kg body weight

per day in a 2-year study in rats for retinal atrophy and inhibition of brain acetylcholinesterase at the higher dose, and using an uncertainty factor of 100. Lower NOAELs in animals, based only on inhibition of erythrocyte or brain acetylcholinesterase, were not considered relevant because of the availability of a NOAEL for erythrocyte acetylcholinesterase inhibition in humans, which was 0.1 mg/kg of body weight per day.

Intake of parathion from all sources is generally low and well below the ADI. As the health-based value is much higher than parathion concentrations likely to be found in drinking-water, the presence of parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a guideline value for parathion is not deemed necessary.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to parathion, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Parathion was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (1996) *Pesticide residues in food – 1995 evaluations. Part II – Toxicological and environmental*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/96.48).

WHO (2003) *Parathion in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/110).

12.97 Pendimethalin

Pendimethalin (CAS No. 40487-42-1) is a pre-emergence herbicide that is fairly immobile and persistent in soil. It is used in large amounts in Japan (5000 tonnes per year). It is lost through photodegradation, biodegradation and volatilization. The leaching potential of pendimethalin appears to be very low, but little is known about its more polar degradation products.

Guideline value	0.02 mg/litre
Occurrence	Rarely been found in drinking-water in the limited studies available (detection limit 0.01 µg/litre)
TDI	5 µg/kg of body weight, based on evidence of slight liver toxicity even at the lowest dose tested (5 mg/kg of body weight) in a long-term rat feeding study, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for a combination of the use of a LOAEL instead of a NOAEL and limitations of the database)
Limit of detection	0.01 µg/litre by GC/MS
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

In a short-term dietary study in rats, a variety of indications of hepatotoxicity as well as increased kidney weights in males were observed at the highest dose level. In a long-term dietary study, some toxic effects (hyperglycaemia in the mouse and hepatotoxicity in the rat) were present even at the lowest dose level. On the basis of available data, pendimethalin does not appear to have significant mutagenic activity. Long-term studies in mice and rats have not provided evidence of carcinogenicity; however, these studies have some important methodological limitations.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to pendimethalin, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Pendimethalin was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for pendimethalin in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Pendimethalin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/41).

12.98 Pentachlorophenol (PCP)

PCP (CAS No. 87-86-5) 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.

Provisional guideline value	0.009 mg/litre The guideline value is considered provisional because of the variations in metabolism between experimental animals and humans.
Occurrence	Concentrations in water samples are usually below 10 µg/litre, although much higher concentrations in groundwater may be measured under certain conditions.
Basis of guideline derivation	Multistage modelling of tumour incidence in a US NTP bioassay without incorporation of a body surface area correction, recognizing that there are interspecies differences in metabolism between animals and humans, with an important metabolite formed in rats being only a minor metabolite in humans
Limit of detection	0.005–0.01 µg/litre by GC with ECD
Treatment achievability	0.4 µg/litre should be achievable using GAC
Additional comments	The concentration of PCP associated with a 10^{-5} upper-bound excess lifetime cancer risk is similar to the guideline value established in the second edition, so that guideline value is retained.

Toxicological review

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.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to PCP, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a health-based guideline value of 0.01 mg/litre was recommended for PCP. The 1993 Guidelines established a health-based guideline value of 0.009 mg/litre for PCP in drinking-water. This value was considered provisional because PCP was evaluated only at the Final Task Group Meeting on the basis of an EHC monograph (No. 71). The concentration of PCP associated

with a 10^{-5} upper-bound excess lifetime cancer risk was found to be similar to the provisional guideline value established in 1993, and so that provisional guideline value was retained in the addendum to the Guidelines, published in 1998.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Pentachlorophenol in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/62).

12.99 Permethrin

Permethrin (CAS No. 52645-53-1) is a contact insecticide effective against a broad range of pests in agriculture, forestry and public health. It has been used as a larvicide to control aquatic invertebrates in water mains. Permethrin is photodegraded both in water and on soil surfaces. In soil, permethrin is rapidly degraded by hydrolysis and microbial action under aerobic conditions. Exposure of the general population to permethrin is mainly via the diet.

Guideline value	0.3 mg/litre (when permethrin is used as a larvicide) This guideline value is applicable where permethrin is applied directly to water as a larvicide. In other situations, it is not considered necessary to derive a health-based guideline value (see Additional comments below).
Occurrence	Concentrations as high as 0.8 mg/litre have been recorded in surface water; in the United Kingdom, levels in drinking-water are below 0.1 µg/litre, but no data were located from elsewhere.
ADI	0.05 mg/kg of body weight, established for technical-grade permethrin with cis : trans ratios of 25 : 75 to 40 : 60 on the basis of a NOAEL of 100 mg/kg, equivalent to 5 mg/kg of body weight per day, in a 2-year study in rats, which was based on clinical signs and changes in body and organ weights and blood chemistry at 500 mg/kg, and a NOAEL of 5 mg/kg of body weight per day in a 1-year study in dogs, based on reduced body weight at 100 mg/kg of body weight per day, and applying an uncertainty factor of 100
Limit of detection	0.05 µg/litre by gas–liquid chromatography with an ECD or FID
Treatment achievability	Permethrin adsorbs to a wide range of materials and is readily removed by conventional treatment methods; neither *cis*- nor *trans*-permethrin reacts with chlorine under normal disinfection conditions.

Guideline derivation	
• allocation to water	20% (where permethrin is used as a larvicide in water)
• weight	60 kg
• consumption	2 litres/day
Additional comments	• A health-based value of 20 µg/litre (rounded value) can be derived by allocating 1% of the ADI to drinking-water, because there is significant exposure to permethrin from food. However, because permethrin usually occurs in drinking-water at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value where permethrin is not added directly to water as a larvicide. • Adding permethrin directly to drinking-water for public health purposes is not recommended by WHO, as part of its policy to exclude the use of any pyrethroids for larviciding of mosquito vectors of human disease. This policy is based on concern over the possible accelerated development of vector resistance to synthetic pyrethroids, which, in their application to insecticide-treated mosquito nets, are crucial in the current global anti-malaria strategy.

Toxicological review

Technical-grade permethrin is of low acute toxicity. The *cis* isomer is considerably more toxic than the *trans* isomer. IARC has classified permethrin in Group 3 (not classifiable as to its carcinogenicity to humans), as there are no human data and only limited data from animal studies. Permethrin is not genotoxic. JMPR has concluded that technical-grade permethrin is not a reproductive or developmental toxin.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to permethrin, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Permethrin was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the second edition of the Guidelines (1993) established a health-based guideline value of 0.02 mg/litre for permethrin in drinking-water, based on an ADI established by JMPR in 1987 for 2:3 and 1:3 *cis*:*trans*-permethrin and recognizing the significant exposure to permethrin from the environment. It was noted that if permethrin is to be used as a larvicide for the control of mosquitoes and other insects of health significance in drinking-water sources, the share of the ADI allocated to drinking-water may be increased.

Assessment date

The risk assessment was conducted in 2004.

Principal references

FAO/WHO (2000) *Pesticide residues in food – 1999. Evaluations – 1999. Part II – Toxicology*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/00.4).

WHO (2005) *Permethrin in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/111).

12.99(a) Petroleum products

Petroleum products are used in large quantities, primarily as fuels. They are complex mixtures of chemicals derived from crude oil by distillation and fractionation. They consist primarily of a wide range of aliphatic and aromatic hydrocarbons, many of which are of extremely low solubility in water. Petroleum products are widely stored and handled and are often spilt. The primary concern for drinking-water is the potential for spills into source water, penetration of distribution systems and contamination of drinking-water treatment works.

Exposure to the constituents of petroleum products through drinking-water is frequently short term, as the result of an accidental spill or short-term incident. Such incidents may lead to high concentrations of total petroleum hydrocarbons (TPH). However, a number of the most soluble aromatic hydrocarbons will be detectable by taste and/or odour at concentrations below those concentrations of concern for health, particularly for short-term exposure. Substances such as the alkyl benzenes and the alkyl naphthalenes have taste and odour thresholds of a few micrograms per litre. In view of the above, it is not considered appropriate to set a formal health-based guideline value for petroleum products in drinking-water.

In the event of a spill, it may be necessary to carry out a context-specific assessment of the risk to health. The fact that petroleum products are complex mixtures of many individual hydrocarbons is a complicating factor in determining the potential risks to consumers. The traditional approach of evaluating individual chemicals in assessing the risks from drinking-water is, therefore, largely inappropriate. In order to overcome this difficulty, it is more practical to consider a series of hydrocarbon fractions and to determine appropriate tolerable concentrations for those fractions. The most widely accepted approach is that developed by the Total Petroleum Hydrocarbons Criteria Working Group in the USA, which divided TPH into a series of aliphatic and aromatic fractions based on the number of carbon atoms and the boiling point, to give equivalent carbon numbers.

This pragmatic approach provides a suitable basis for assessing the potential health risks associated with larger-scale contamination of drinking-water by petroleum products. The allocation of 10% of each of the reference doses, equivalent to TDIs, for the various fractions to drinking-water provides a conservative assessment of the risks. Although the approach is based on the analysis of hydrocarbon fractions, most

are of low solubility, and the most soluble fractions, consisting largely of lower molecular weight aromatic hydrocarbons, will be present in the greatest concentration.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first, second and third editions of the *Guidelines for Drinking-water Quality* did not refer to petroleum products in general, although guideline values have been established for individual petroleum hydrocarbons (e.g., benzene, ethylbenzene, toluene, xylenes) and individual polycyclic aromatic hydrocarbon contaminants of petroleum products (e.g., benzo(*a*)pyrene).

Assessment date

The risk assessment was conducted in 2004.

Principal reference

WHO (2005) *Petroleum products in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/123).

12.100 pH

No health-based guideline value is proposed for pH. Although pH usually has no direct impact on consumers, it is one of the most important operational water quality parameters (see chapter 10).

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that pH less than 6.5 or greater than 9.2 would markedly impair the potability of the water. The 1963 and 1971 International Standards retained the pH range 6.5–9.2 as the allowable or permissible range. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value pH range of 6.5–8.5 was established for pH, based on aesthetic considerations. It was noted that the acceptable range of pH may be broader in the absence of a distribution system. No health-based guideline value was proposed for pH in the 1993 Guidelines. Although pH usually has no direct impact on consumers, it is one of the most important operational water quality parameters, the optimum pH required often being in the range 6.5–9.5.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *pH in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/12).

12.101 2-Phenylphenol and its sodium salt

2-Phenylphenol (CAS No. 90-43-7) is used as a disinfectant, bactericide and virucide. In agriculture, it is used in disinfecting fruits, vegetables and eggs. It is also used as a general surface disinfectant in hospitals, nursing homes, veterinary hospitals, poultry farms, dairy farms, commercial laundries, barbershops and food processing plants. 2-Phenylphenol is readily degraded in surface waters, with a half-life of about 1 week in river water.

2-Phenylphenol has been determined to be of low toxicity. Both 2-phenylphenol and its sodium salt are carcinogenic in male rats, and 2-phenylphenol is carcinogenic in male mice. However, urinary bladder tumours observed in male rats and liver tumours observed in male mice exposed to 2-phenylphenol appear to be threshold phenomena that are species- and sex-specific. JMPR has concluded that 2-phenylphenol is unlikely to represent a carcinogenic risk to humans. Although a working group convened by IARC has classified 2-phenylphenol, sodium salt, in Group 2B (possibly carcinogenic to humans) and 2-phenylphenol in Group 3 (not classifiable as to its carcinogenicity to humans), JMPR noted that the IARC classification is based on hazard identification, not risk assessment, and is furthermore limited to published literature, excluding unpublished studies on toxicity and carcinogenicity. JMPR also concluded that there are unresolved questions about the genotoxic potential of 2-phenylphenol.

A health-based value of 1 mg/litre can be calculated for 2-phenylphenol on the basis of an ADI of 0.4 mg/kg of body weight, based on a NOAEL of 39 mg/kg of body weight per day in a 2-year toxicity study for decreased body weight gain and hyperplasia of the urinary bladder and carcinogenicity of the urinary bladder in male rats, using an uncertainty factor of 100. Because of its low toxicity, however, the health-based value derived for 2-phenylphenol is much higher than 2-phenylphenol concentrations likely to be found in drinking-water. Under usual conditions, therefore, the presence of 2-phenylphenol in drinking-water is unlikely to represent a hazard to human health. For this reason, the establishment of a guideline value for 2-phenylphenol is not deemed necessary.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to 2-phenylphenol, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 2-Phenylphenol was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*,

published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2000) *Pesticide residues in food – 1999 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/00.4).

WHO (2003) *2-Phenylphenol and its sodium salt in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/69).

12.102 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. Fluoranthene 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. 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 charbroiling, 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 equal or even exceed that from food.

Guideline value for benzo[a]pyrene (BaP)	0.0007 mg/litre (0.7 µg/litre)
Occurrence	PAH levels in uncontaminated groundwater usually in range 0–5 ng/litre; concentrations in contaminated groundwater may exceed 10 µg/litre; typical concentration range for sum of selected PAHs in drinking-water is from about 1 ng/litre to 11 µg/litre

Basis of guideline derivation	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
Limit of detection	0.01 µg/litre by GC/MS and reverse-phase HPLC with a fluorescence detector
Treatment achievability	0.05 µg/litre should be achievable using coagulation
Additional comments	• The presence of significant concentrations of BaP in drinking-water in the absence of very high concentrations of fluoranthene 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.

Toxicological review

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. 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.

A health-based value of 4 µg/litre can be calculated for fluoranthene on the basis of a NOAEL of 125 mg/kg of body weight per day for increased serum glutamate–pyruvate transaminase levels, kidney and liver pathology, and clinical and haematological changes in a 13-week oral gavage study in mice, using an uncertainty factor of 10 000 (100 for inter- 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). However, this health-based value is significantly above the concentrations normally found in drinking-water. Under usual conditions, therefore, the presence of fluoranthene in drinking-water does not represent a hazard to human health. For this reason, the establishment of a guideline value for fluoranthene is not deemed necessary.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to PAHs. The 1971 International Standards stated that some PAHs are known to be carcinogenic and that the concentrations of six representative PAH compounds (fluoranthene, 3,4-benzfluoranthene, 11,12-benzfluoranthene, 3,4-benzpyrene, 1,12-benzpyrene and indeno [1,2,3-cd] pyrene) should therefore not, in general, exceed 0.0002 mg/litre. In the first edition of the *Guidelines for Drinking-water Quality*,

published in 1984, the only PAH for which there was sufficient substantiated toxicological evidence to set a guideline value was BaP. A health-based guideline value of 0.00001 mg/litre was recommended for BaP, while noting that the mathematical model appropriate to chemical carcinogens that was used in its derivation involved considerable uncertainty. It was also recommended that the control of PAHs in drinking-water should be based on the concept that the levels found in unpolluted groundwater should not be exceeded. The 1993 Guidelines concluded that there were insufficient data available to derive drinking-water guidelines for PAHs other than BaP. The guideline value for BaP, corresponding to an upper-bound excess lifetime cancer risk of 10^{-5}, was calculated to be 0.0007 mg/litre. This guideline value was retained in the addendum to the second edition of the Guidelines, published in 1998, as it was confirmed by new studies on the carcinogenicity of the compound. It was also recommended that the use of coal-tar-based and similar materials for pipe linings and coatings on storage tanks be discontinued. Although a health-based value for fluoranthene was calculated in the addendum, it was significantly above the concentrations found in drinking-water, and it was concluded that, under usual conditions, the presence of fluoranthene in drinking-water does not represent a hazard to human health; thus, the establishment of a guideline value for fluoranthene was not deemed necessary. As there are few data on the oral toxicity of other PAHs, particularly in drinking-water, relative potencies of carcinogenic PAHs were determined by comparison of data from dermal and other studies, which provides a useful indicator of PAH potency relative to BaP.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Polynuclear aromatic hydrocarbons in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/59).

12.103 Propanil

Propanil (CAS No. 709-98-8) is a contact post-emergence herbicide used to control broad-leaved and grassy weeds, mainly in rice. It is a mobile compound with affinity for the water compartment. Propanil is not, however, persistent, being easily transformed under natural conditions to several metabolites. Two of these metabolites, 3,4-dichloroaniline and 3,3′,4,4′-tetrachloroazobenzene, are more toxic and more persistent than the parent compound. Although used in a number of countries, propanil has only occasionally been detected in groundwater.

Although a health-based value for propanil can be derived, this has not been done, because propanil is readily transformed into metabolites that are more toxic. Therefore, a guideline value for the parent compound is considered inappropriate, and there are inadequate data on the metabolites to allow the derivation of a guideline value for them. Authorities should consider the possible presence in water of more toxic environmental metabolites.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to propanil, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Propanil was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for propanil in drinking-water, noting that in applying this guideline, authorities should consider the possible presence of more toxic metabolites in water.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Propanil in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/112).

12.104 Pyriproxyfen

Pyriproxyfen (CAS No. 95737-68-1) is a broad-spectrum insect growth regulator with insecticidal activity against public health insect pests. It is a WHOPES-recommended insecticide for the control of mosquito larvae. In agriculture and horticulture, pyriproxyfen has registered uses for the control of scale, whitefly, bollworm, jassids, aphids and cutworms. Pyriproxyfen degrades rapidly in soil under aerobic conditions, with a half-life of 6.4–36 days. It disappeared from aerobic lake water–sediment systems with half-lives of 16 and 21 days. Pyriproxyfen appeared to be degraded much more slowly in anaerobic lake water–sediment systems. As pyriproxyfen is a new pesticide, few environmental data have been collected. Intake of pyriproxyfen from all sources is generally low and below the ADI.

Guideline value	0.3 mg/litre
Occurrence	No detectable concentrations found in surface water in the USA
ADI	0.1 mg/kg of body weight based on an overall NOAEL of 10 mg/kg of body weight per day for increased relative liver weight and increased total plasma cholesterol concentration in male dogs in two 1-year toxicity studies, using an uncertainty factor of 100
Limit of detection	No information found
Treatment achievability	No data available; 1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of ADI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

JMPR concluded that pyriproxyfen was not carcinogenic or genotoxic. In short- and long-term studies of the effects of pyriproxyfen in mice, rats and dogs, the liver (increases in liver weight and changes in plasma lipid concentrations, particularly cholesterol) was the main toxicological target.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to pyriproxyfen, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Pyriproxyfen was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, in the second edition, published in 1993, or in the addendum to the second edition, published in 1998.

Assessment date

The risk assessment was conducted in 2003.

Principal references

FAO/WHO (2000) *Pesticide residues in food – 1999 evaluations. Part II – Toxicological*. Geneva, World Health Organization, Joint FAO/WHO Meeting on Pesticide Residues (WHO/PCS/00.4).

WHO (2003) *Pyriproxyfen in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/113).

12.105 Selenium

Selenium is present in the Earth's crust, often in association with sulfur-containing minerals. Selenium is an essential trace element, and foodstuffs such as cereals, meat

and fish are the principal source of selenium in the general population. Levels in food also vary greatly according to geographical area of production.

Guideline value	0.01 mg/litre
Occurrence	Levels in drinking-water vary greatly in different geographical areas but are usually much less than 0.01 mg/litre.
NOAEL in humans	Estimated to be about 4 µg/kg of body weight per day, based on data in which a group of 142 persons with a mean daily intake of 4 µg/kg body weight showed no clinical or biochemical signs of selenium toxicity
Limit of detection	0.5 µg/litre by AAS with hydride generation
Treatment achievability	0.01 mg/litre should be achievable using coagulation for selenium(IV) removal; selenium(VI) is not removed by conventional treatment processes
Guideline derivation	
• allocation to wate	10% of NOAEL
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Selenium is an essential element for humans, with a recommended daily intake of about 1 µg/kg of body weight for adults. Selenium compounds have been shown to be genotoxic in *in vitro* systems with metabolic activation, but not in humans. There was no evidence of teratogenic effects in monkeys. Long-term toxicity in rats is characterized by depression of growth and liver pathology. In humans, the toxic effects of long-term selenium exposure are manifested in nails, hair and liver. Data from China indicate that clinical and biochemical signs occur at a daily intake above 0.8 mg. Daily intakes of Venezuelan children with clinical signs were estimated to be about 0.7 mg on the basis of their blood levels and the Chinese data on the relationship between blood level and intake. Effects on synthesis of a liver protein were also seen in a small group of patients with rheumatoid arthritis given selenium at a rate of 0.25 mg/day in addition to selenium from food. No clinical or biochemical signs of selenium toxicity were reported in a group of 142 persons with a mean daily intake of 0.24 mg (maximum 0.72 mg) from food.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.05 mg/litre for selenium, based on health concerns. In the 1963 International Standards, this value was lowered to 0.01 mg/litre, which was retained in the 1971 International Standards as a tentative upper concentration limit, while recognizing that selenium is an essential trace element for some species. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, the guideline value of 0.01 mg/litre was again retained, although it was noted that in areas of

relatively higher or lower selenium dietary intake, the guideline value may have to be modified accordingly. The 1993 Guidelines proposed a health-based guideline value of 0.01 mg/litre on the basis of human studies.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Selenium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/13).

12.106 Silver

Silver occurs naturally mainly in the form of its very insoluble and immobile oxides, sulfides and some salts. It has occasionally been found in groundwater, surface water and drinking-water at concentrations above 5 µg/litre. Levels in drinking-water treated with silver for disinfection may be above 50 µg/litre. Recent estimates of daily intake are about 7 µg per person.

Only a small percentage of silver is absorbed. Retention rates in humans and laboratory animals range between 0 and 10%.

The only obvious sign of silver overload is argyria, a condition in which skin and hair are heavily discoloured by silver in the tissues. An oral NOAEL for argyria in humans for a total lifetime intake of 10 g of silver was estimated on the basis of human case reports and long-term animal experiments.

The low levels of silver in drinking-water, generally below 5 µg/litre, are not relevant to human health with respect to argyria. On the other hand, special situations exist where silver salts may be used to maintain the bacteriological quality of drinking-water. Higher levels of silver, up to 0.1 mg/litre (this concentration gives a total dose over 70 years of half the human NOAEL of 10 g), could be tolerated in such cases without risk to health.

There are no adequate data with which to derive a health-based guideline value for silver in drinking-water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to silver. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was not considered necessary to establish a guideline value for silver in drinking-water. No health-based guideline value for silver was proposed in the 1993 Guidelines. Where silver salts are used to maintain the bacteriological quality of

drinking-water, levels of silver up to 0.1 mg/litre can be tolerated without risk to health.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Silver in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/14).

12.107 Simazine

Simazine (CAS No. 122-34-9) is a pre-emergence herbicide used on a number of crops as well as in non-crop areas. It is fairly resistant to physical and chemical dissipation processes in the soil. It is persistent and mobile in the environment.

Guideline value	0.002 mg/litre
Occurrence	Frequently detected in groundwater and surface water at concentrations of up to a few micrograms per litre
TDI	0.52 µg/kg of body weight, based on a NOAEL of 0.52 mg/kg of body weight from a long-term study in the rat (based on weight changes, effects on haematological parameters and an increase in mammary tumours) and an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for possible non-genotoxic carcinogenicity)
Limit of detection	0.01 µg/litre by GC/MS; 0.1–0.2 µg/litre by GC with flame thermionic detection
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Simazine does not appear to be genotoxic in mammalian systems. Recent studies have shown an increase in mammary tumours in the female rat but no effects in the mouse. IARC has classified simazine in Group 3.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to simazine, but the 1971 International Standards suggested that pesticide residues that

may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Simazine was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.002 mg/litre for simazine in drinking-water.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Simazine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/42).

12.108 Sodium

Sodium salts (e.g., sodium chloride) are found in virtually all food (the main source of daily exposure) and drinking-water. Although concentrations of sodium in potable water are typically less than 20 mg/litre, they can greatly exceed this in some countries. The levels of sodium salts in air are normally low in relation to those in food or water. It should be noted that some water softeners can add significantly to the sodium content of drinking-water.

No firm conclusions can be drawn concerning the possible association between sodium in drinking-water and the occurrence of hypertension. Therefore, no health-based guideline value is proposed. However, concentrations in excess of 200 mg/litre may give rise to unacceptable taste (see chapter 10).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to sodium. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that there was insufficient evidence to justify a guideline value for sodium in water based on health risk considerations, but it was noted that intake of sodium from drinking-water may be of greater significance in persons who require a sodium-restricted diet and bottle-fed infants. A guideline value of 200 mg/litre was established for sodium based on taste considerations. No health-based guideline value was proposed for sodium in the 1993 Guidelines, as no firm conclusions could be drawn concerning the possible association between sodium in drinking-water and the occurrence of hypertension. However, concentrations in excess of 200 mg/litre may give rise to unacceptable taste.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Sodium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/15).

12.109 Styrene

Styrene, which is used primarily for the production of plastics and resins, is found in trace amounts in surface water, drinking-water and food. In industrial areas, exposure via air can result in intake of a few hundred micrograms per day. Smoking may increase daily exposure by up to 10-fold.

Guideline value	0.02 mg/litre
Occurrence	Has been detected in drinking-water and surface water at concentrations below 1 µg/litre
TDI	7.7 µg/kg of body weight, based on a NOAEL of 7.7 mg/kg of body weight per day for decreased body weight observed in a 2- year drinking-water study in rats, and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the carcinogenicity and genotoxicity of the reactive intermediate styrene-7,8-oxide)
Limit of detection	0.3 µg/litre by GC with photoionization detection and confirmation by MS
Treatment achievability	0.02 mg/litre may be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	Styrene may affect the acceptability of drinking-water at the guideline value.

Toxicological review

Following oral or inhalation exposure, styrene is rapidly absorbed and widely distributed in the body, with a preference for lipid depots. It is metabolized to the active intermediate styrene-7,8-oxide, which is conjugated with glutathione or further metabolized. Metabolites are rapidly and almost completely excreted in urine. Styrene has a low acute toxicity. In short-term toxicity studies in rats, impairment of glutathione transferase activity and reduced glutathione concentrations were observed. In *in vitro* tests, styrene has been shown to be mutagenic in the presence of metabolic

activation only. In *in vitro* as well as in *in vivo* studies, chromosomal aberrations have been observed, mostly at high doses of styrene. The reactive intermediate styrene-7,8-oxide is a direct-acting mutagen. In long-term studies, orally administered styrene increased the incidence of lung tumours in mice at high dose levels but had no carcinogenic effect in rats. Styrene-7,8-oxide was carcinogenic in rats after oral administration. IARC has classified styrene in Group 2B. The available data suggest that the carcinogenicity of styrene is due to overloading of the detoxification mechanism for styrene-7,8-oxide (e.g., glutathione depletion).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to styrene. The 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for styrene, noting that styrene may affect the acceptability of drinking-water at this concentration.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Styrene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/27).

12.110 Sulfate

Sulfates occur naturally in numerous minerals and are used commercially, principally in the chemical industry. They are discharged into water in industrial wastes and through atmospheric deposition; however, the highest levels usually occur in groundwater and are from natural sources. In general, the average daily intake of sulfate from drinking-water, air and food is approximately 500 mg, food being the major source. However, in areas with drinking-water supplies containing high levels of sulfate, drinking-water may constitute the principal source of intake.

The existing data do not identify a level of sulfate in drinking-water that is likely to cause adverse human health effects. The data from a liquid diet piglet study and from tap water studies with human volunteers indicate a laxative effect at concentrations of 1000–1200 mg/litre but no increase in diarrhoea, dehydration or weight loss.

No health-based guideline is proposed for sulfate. However, because of the gastrointestinal effects resulting from ingestion of drinking-water containing high sulfate levels, it is recommended that health authorities be notified of sources of drinking-water that contain sulfate concentrations in excess of 500 mg/litre. The presence of

sulfate in drinking-water may also cause noticeable taste (see chapter 10) and may contribute to the corrosion of distribution systems.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of sulfate greater than 400 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. The first two editions of the International Standards also suggested that concentrations of magnesium plus sodium sulfate in excess of 1000 mg/litre would markedly impair drinking-water potability. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 400 mg/litre for sulfate was established, based on taste considerations. No health-based guideline value for sulfate was proposed in the 1993 Guidelines. However, because of the gastrointestinal effects resulting from ingestion of drinking-water containing high sulfate levels, it was recommended that health authorities be notified of sources of drinking-water that contain sulfate concentrations in excess of 500 mg/litre. The presence of sulfate in drinking-water may also cause noticeable taste at concentrations above 250 mg/litre and may contribute to the corrosion of distribution systems.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Sulfate in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/114).

12.111 2,4,5-T (2,4,5-Trichlorophenoxyacetic acid)

The half-lives for degradation of chlorophenoxy herbicides, including 2,4,5-T (CAS No. 93-76-5), in the environment are in the order of several days. Chlorophenoxy herbicides are not often found in food.

Guideline value	0.009 mg/litre
Occurrence	Chlorophenoxy herbicides not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre
TDI	3 µg/kg of body weight, based on a NOAEL of 3 mg/kg of body weight for reduced body weight gain, increased liver and kidney weights and renal toxicity in a 2-year study in rats, with an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 to take into consideration the suggested association between 2,4,5-T and soft tissue sarcoma and non- Hodgkin lymphoma in epidemiological studies)

Limit of detection	0.02 µg/litre by GC with an ECD
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

Chlorophenoxy herbicides, as a group, have been classified in Group 2B by IARC. However, the available data from studies in exposed populations and animals do not permit assessment of the carcinogenic potential to humans of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. The NOAEL for reproductive effects (reduced neonatal survival, decreased fertility, reduced relative liver weights and thymus weights in litters) of dioxin-free (<0.03 µg/kg) 2,4,5-T in a three-generation reproduction study in rats is the same as the NOAEL for reduced body weight gain, increased liver and kidney weights and renal toxicity in a toxicity study in which rats were fed 2,4,5-T (practically free from dioxin contamination) in the diet for 2 years.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to chlorophenoxy herbicides, including 2,4,5-T, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. 2,4,5-T was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.009 mg/litre for 2,4,5-T.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Chlorophenoxy herbicides (excluding 2,4-D and MCPA) in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/44).

12.112 Terbuthylazine (TBA)

TBA (CAS No. 5915-41-3), 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.

Guideline value	0.007 mg/litre
Occurrence	Concentrations in water seldom exceed 0.2 µg/litre, although higher concentrations have been observed.
TDI	2.2 µg/kg of body weight, based on a NOAEL of 0.22 mg/kg of body weight for decreased body weight gain at the next higher dose in a 2-year toxicity/carcinogenicity study in rats, with an uncertainty factor of 100 (for inter- and intraspecies variation)
Limit of detection	0.1 µg/litre by HPLC with UV detection
Treatment achievability	0.1 µg/litre should be achievable using GAC
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

There is no evidence that TBA is carcinogenic or mutagenic. In long-term dietary studies in rats, effects on red blood cell parameters in females, an increased incidence of non-neoplastic lesions in the liver, lung, thyroid and testis and a slight decrease in body weight gain were observed.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to TBA, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value for triazine herbicides, which include TBA, was recommended after a detailed evaluation of the compounds. TBA was not evaluated in the second edition of the *Guidelines for Drinking-water Quality*, published in 1993. In the addendum to the second edition of the Guidelines, published in 1998, a health-based guideline value of 0.007 mg/litre was derived for TBA in drinking-water.

Assessment date

The risk assessment was originally conducted in 1998. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Terbuthylazine in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/63).

12.113 Tetrachloroethene

Tetrachloroethene has been used primarily as a solvent in dry cleaning industries and to a lesser extent as a degreasing solvent. It is widespread in the environment and is found in trace amounts in water, aquatic organisms, air, foodstuffs and human tissue. The highest environmental levels of tetrachloroethene are found in the commercial dry cleaning and metal degreasing industries. Emissions can sometimes lead to high concentrations in groundwater. Tetrachloroethene in anaerobic groundwater may degrade to more toxic compounds, including vinyl chloride.

Guideline value	0.04 mg/litre
Occurrence	Concentrations in drinking-water are generally below 3 µg/litre, although much higher concentrations have been detected in well water (23 mg/litre) and in contaminated groundwater (1 mg/litre).
TDI	14 µg/kg of body weight, based on hepatotoxic effects observed in a 6-week gavage study in male mice and a 90-day drinking-water study in male and female rats, and taking into consideration carcinogenic potential (but not the short length of the study, in view of the database and considerations regarding the application of the dose via drinking-water in one of the two critical studies)
Limit of detection	0.2 µg/litre by GC with ECD; 4.1 µg/litre by GC/MS
Treatment achievability	0.001 mg/litre should be achievable using air stripping
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day

Toxicological review

At high concentrations, tetrachloroethene causes central nervous system depression. Lower concentrations of tetrachloroethene have been reported to damage the liver and the kidneys. IARC has classified tetrachloroethene in Group 2A. Tetrachloroethene has been reported to produce liver tumours in male and female mice, with some evidence of mononuclear cell leukaemia in male and female rats and kidney tumours in male rats. The overall evidence from studies conducted to assess the genotoxicity of tetrachloroethene, including induction of single-strand DNA breaks, mutation in germ cells and chromosomal aberrations *in vitro* and *in vivo*, indicates that tetrachloroethene is not genotoxic.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to tetrachloroethene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a tentative guideline value of 0.01 mg/litre was recommended; the guideline was designated as tentative because, although the carcinogenicity data did not justify a full guideline value, the compound was considered to have important health implications when present in drinking-water. The 1993 Guidelines established a health-based guideline value of 0.04 mg/litre for tetrachloroethene.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Tetrachloroethene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/23).

12.114 Toluene

Most toluene (in the form of benzene–toluene–xylene mixtures) is used in the blending of petrol. It is also used as a solvent and as a raw material in chemical production. The main exposure is via air. Exposure is increased by smoking and in traffic.

Guideline value	0.7 mg/litre
Occurrence	Concentrations of a few micrograms per litre have been found in surface water, groundwater and drinking-water; point emissions can lead to higher concentrations in groundwater (up to 1 mg/litre). It may also penetrate plastic pipes from contaminated soil.
TDI	223 µg/kg of body weight, based on a LOAEL of 312 mg/kg of body weight per day for marginal hepatotoxic effects observed in a 13-week gavage study in mice, correcting for 5 days per week dosing and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the short duration of the study and use of a LOAEL instead of a NOAEL)
Limit of detection	0.13 µg/litre by GC with FID; 6 µg/litre by GC/MS
Treatment achievability	0.001 mg/litre should be achievable using air stripping
Guideline derivation	
• allocation to water	10% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	The guideline value exceeds the lowest reported odour threshold for toluene in water.

Toxicological review

Toluene is absorbed completely from the gastrointestinal tract and rapidly distributed in the body, with a preference for adipose tissue. Toluene is rapidly metabolized and, following conjugation, excreted predominantly in urine. With occupational exposure to toluene by inhalation, impairment of the central nervous system and irritation of mucous membranes are observed. The acute oral toxicity is low. Toluene exerts embryotoxic and fetotoxic effects, but there is no clear evidence of teratogenic activity in laboratory animals and humans. In long-term inhalation studies in rats and mice, there is no evidence for carcinogenicity of toluene. Genotoxicity tests *in vitro* were negative, whereas *in vivo* assays showed conflicting results with respect to chromosomal aberrations. IARC has concluded that there is inadequate evidence for the carcinogenicity of toluene in both experimental animals and humans and classified it as Group 3 (not classifiable as to its carcinogenicity to humans).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to toluene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended after a detailed evaluation of the compound. The 1993 Guidelines established a health-based guideline value of 0.7 mg/litre for toluene, but noted that this value exceeds the lowest reported odour threshold for toluene in water (0.024 mg/litre).

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Toluene in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/116).

12.115 Total dissolved solids (TDS)

TDS comprise inorganic salts (principally calcium, magnesium, potassium, sodium, bicarbonates, chlorides and sulfates) and small amounts of organic matter that are dissolved in water. TDS in drinking-water originate from natural sources, sewage, urban runoff and industrial wastewater. Salts used for road de-icing in some countries may also contribute to the TDS content of drinking-water. Concentrations of TDS in water vary considerably in different geological regions owing to differences in the solubilities of minerals.

Reliable data on possible health effects associated with the ingestion of TDS in drinking-water are not available, and no health-based guideline value is proposed. However, the presence of high levels of TDS in drinking-water may be objectionable to consumers (see chapter 10).

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of total solids greater than 1500 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 1000 mg/litre was established for TDS, based on taste considerations. No health-based guideline value for TDS was proposed in the 1993 Guidelines, as reliable data on possible health effects associated with the ingestion of TDS in drinking-water were not available. However, the presence of high levels of TDS in drinking-water (greater than 1200 mg/litre) may be objectionable to consumers. Water with extremely low concentrations of TDS may also be unacceptable because of its flat, insipid taste.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Total dissolved solids in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/16).

12.116 Trichloroacetic acid

Chlorinated acetic acids are formed from organic material during water chlorination.

Guideline value	0.2 mg/litre
Occurrence	Detected in US groundwater and surface water distribution systems at mean concentrations of 5.3 µg/litre (range <1.0–80 µg/litre) and 16 µg/litre (range <1.0–174 µg/litre), respectively; maximum concentration (200 µg/litre) measured in chlorinated water in Australia
TDI	32.5 µg/kg of body weight, based on a NOAEL of 32.5 mg/kg of body weight per day from a study in which decreased body weight, increased liver serum enzyme activity and liver histopathology were seen in rats exposed to trichloroacetate in drinking-water for 2 years, incorporating an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for database deficiencies, including the absence of a multigeneration reproductive study, the lack of a developmental study in a second species and the absence of full histopathological data in a second species)
Limit of detection	1 µg/litre by GC with ECD; 1 µg/litre by GC/MS

Treatment achievability	Trichloroacetic acid concentrations in drinking-water are generally below 0.1 mg/litre. Concentrations may be reduced by installing or optimizing coagulation to remove precursors and/or by controlling the pH during chlorination.
Guideline derivation	
• allocation to water	20% of TDI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	A similar TDI for trichloroacetate was established by IPCS based on a NOAEL for hepatic toxicity in a long-term study in mice.

Toxicological review

Trichloroacetic acid has been shown to induce tumours in the liver of mice. It has given mixed results in *in vitro* assays for mutations and chromosomal aberrations and has been reported to cause chromosomal aberrations in *in vivo* studies. IARC has classified trichloroacetic acid in Group 3, not classifiable as to its carcinogenicity to humans. The weight of evidence indicates that trichloroacetic acid is not a genotoxic carcinogen.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to trichloroacetic acid. In the 1993 Guidelines, a provisional guideline value of 0.1 mg/litre was derived for trichloroacetic acid, with the provisional designation because of the limitations of the available toxicological database and because there were inadequate data to judge whether the guideline value was technically achievable. It was emphasized that difficulties in meeting the guideline value must never be a reason for compromising adequate disinfection.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Trichloroacetic acid in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/120).

12.117 Trichlorobenzenes (total)

Releases of trichlorobenzenes (TCBs) into the environment occur through their manufacture and use as industrial chemicals, chemical intermediates and solvents. TCBs are found in drinking-water, but rarely at levels above 1 µg/litre. General population exposure will primarily result from air and food.

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

A health-based value of 20 µg/litre can be calculated for total TCBs on the basis of a TDI of 7.7 µg/kg of body weight, based on liver toxicity identified in a 13-week rat study, taking into consideration the short duration of the study. However, because TCBs occur at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value. It should be noted that the health-based value exceeds the lowest reported odour threshold in water.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to TCBs. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that insufficient health data were available from which to derive a guideline value for 1,2,4-TCB. The 1993 Guidelines proposed a health-based guideline value of 0.02 mg/litre for total TCBs, because of the similarity in the toxicity of the three isomers, but noted that this value exceeds the lowest reported odour threshold in water (0.005 mg/litre for 1,2,4-TCB).

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Trichlorobenzenes in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/117).

12.118 1,1,1-Trichloroethane

1,1,1-Trichloroethane is widely used as a cleaning solvent for electrical equipment, as a solvent for adhesives, coatings and textile dyes and as a coolant and lubricant. It is found mainly in the atmosphere, although it is mobile in soils and readily migrates to groundwaters. 1,1,1-Trichloroethane has been found in only a small proportion of surface waters and groundwaters, usually at concentrations of less than 20 µg/litre; higher concentrations (up to 150 µg/litre) have been observed in a few instances. There appears to be increasing exposure to 1,1,1-trichloroethane from other sources.

1,1,1-Trichloroethane is rapidly absorbed from the lungs and gastrointestinal tract, but only small amounts – about 6% in humans and 3% in experimental animals – are metabolized. Exposure to high concentrations can lead to hepatic steatosis (fatty liver) in both humans and laboratory animals. In a well conducted oral study in mice and rats, effects included reduced liver weight and changes in the kidney consistent

with hyaline droplet neuropathy. IARC has placed 1,1,1-trichloroethane in Group 3. 1,1,1-Trichloroethane does not appear to be mutagenic.

A health-based value of 2 mg/litre can be calculated for 1,1,1-trichloroethane on the basis of a TDI of 0.6 mg/kg of body weight, based on changes in the kidney that were consistent with hyaline droplet nephropathy observed in a 13-week oral study in male rats, and taking into account the short duration of the study. However, because 1,1,1-trichloroethane occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to 1,1,1-trichloroethane. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended after a detailed evaluation of the compound. The 1993 Guidelines proposed a provisional guideline value of 2 mg/litre for 1,1,1-trichloroethane. The value was provisional because it was based on an inhalation study rather than an oral study. It was strongly recommended that an adequate oral toxicity study be conducted to provide more acceptable data for the derivation of a guideline value.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *1,1,1-Trichloroethane in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/65).

12.119 Trichloroethene

Trichloroethene is used primarily in metal degreasing. It is emitted mainly to the atmosphere, but it may also be introduced into groundwater and, to a lesser extent, surface water in industrial effluents. Poor handling as well as improper disposal of trichloroethene in landfills have been the main causes of groundwater contamination. It is expected that exposure to trichloroethene from air will be greater than that from food or drinking-water, unless the drinking-water contains trichloroethene at levels above about 10 µg/litre.

Provisional guideline value	0.02 mg/litre The guideline value is designated as provisional because of deficiencies in the toxicological database.
Occurrence	Due to its high volatility, concentrations are normally low (<1 µg/litre) in surface water; concentrations may be higher (usually below 100 µg/litre) in groundwater systems where volatilization and biodegradation are limited.

TDI	1.46 µg/kg of body weight per day in a developmental toxicity study in rats, based on a $BMDL_{10}$ (the lower 95% confidence limit corresponding to a 10% increase in extra risk of fetal heart malformations over background) of 0.146 mg/kg of body weight per day and using an uncertainty factor of 100 for intra- and interspecies variation
Limit of detection	0.01–3.0 µg/litre by purge and trap capillary GC with photoionization detectors or with photoionization detectors and ECD in series; 0.5 µg/litre by purge and trap capillary GC with MS; 0.01 µg/litre by liquid–liquid extraction and GC with ECD; practical quantification limit considered to be achievable by most good laboratories is 5 µg/litre
Treatment achievability	0.002 mg/litre should be achievable by air stripping, possibly in combination with GAC adsorption
Guideline derivation • allocation to water • weight • consumption	 50% of TDI 60-kg adult 2 litres/day
Additional comments	• The guideline value is protective for both cancer and non-cancer end-points. • In countries with low rates of ventilation in houses and high rates of showering and bathing, authorities may wish to take the additional exposures through the dermal and inhalation routes into consideration in developing national standards from the provisional guideline value.

Toxicological review

Although trichloroethene appears to be weakly genotoxic in *in vitro* and *in vivo* assays, several of its metabolites are genotoxic, and some are established as known or likely human carcinogens. In view of the sufficient weight of evidence of carcinogenicity in two species of experimental animals with supporting human data, IARC classified trichloroethene as Group 2A (probably carcinogenic to humans). Developmental toxicity is considered to be the critical non-cancer effect, because of the low adverse effect level, the severity of the end-point (heart malformations) and the presence of evidence for similar effects (e.g., cardiac anomalies) from epidemiological studies.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to trichloroethene. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a tentative guideline value of 0.03 mg/litre was recommended; the guideline was designated as tentative because, although carcinogenicity was observed in one species only, the compound occurs relatively frequently in drinking-water. The second edition of the Guidelines (1993) established a provisional health-based guideline value of 0.07 mg/litre for trichloroethene. The value was provisional because an uncertainty factor of 3000 was used in its derivation. This guideline value was brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal reference

WHO (2005) *Trichloroethene in drinking-water. Background document for development of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/05.08/22).

12.120 Trifluralin

Trifluralin (CAS No. 1582-09-8) is a pre-emergence herbicide used in a number of crops. It has low water solubility and a high affinity for soil. However, biodegradation and photodegradation processes may give rise to polar metabolites that may contaminate drinking-water sources. Although this compound is used in many countries, relatively few data are available concerning contamination of drinking-water.

Guideline value	0.02 mg/litre
Occurrence	Not detected in the small number of drinking-water samples analysed; has been detected in surface water at concentrations above 0.5 µg/litre and rarely in groundwater
TDI	7.5 µg/kg of body weight, based on a NOAEL of 0.75 mg/kg of body weight for mild hepatic effects in a 1-year feeding study in dogs, with an uncertainty factor of 100 (for inter- and intraspecies variation)
Limit of detection	0.05 µg/litre by GC with nitrogen–phosphorus detection
Treatment achievability	1 µg/litre should be achievable using GAC
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day
Additional comments	Authorities should note that some impure technical grades of trifluralin could contain potent carcinogenic compounds and therefore should not be used.

Toxicological review

Trifluralin of high purity does not possess mutagenic properties. Technical trifluralin of low purity may contain nitroso contaminants and has been found to be mutagenic. No evidence of carcinogenicity was demonstrated in a number of long-term toxicity/carcinogenicity studies with pure (99%) test material. IARC recently evaluated technical-grade trifluralin and assigned it to Group 3.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to trifluralin, but the 1971 International Standards suggested that pesticide residues that may occur in community water supplies make only a minimal contribution to the total daily intake of pesticides for the population served. Trifluralin was not evaluated in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, but the 1993 Guidelines established a health-based guideline value of 0.02 mg/litre for trifluralin in drinking-water, noting that authorities should be aware that some impure technical grades of trifluralin could contain potent carcinogenic compounds and therefore should not be used.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Trifluralin in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/43).

12.121 Trihalomethanes (bromoform, bromodichloromethane, dibromochloromethane, chloroform)

Trihalomethanes (THMs) are formed in drinking-water primarily as a result of chlorination of organic matter present naturally in raw water supplies. The rate and degree of THM formation increase as a function of the chlorine and humic acid concentration, temperature, pH and bromide ion concentration. Chloroform is the most common THM and the principal DBP in chlorinated drinking-water. In the presence of bromides, brominated THMs are formed preferentially and chloroform concentrations decrease proportionally. It is assumed that most THMs present in water are ultimately transferred to air as a result of their volatility. For chloroform, for example, individuals may be exposed during showering to elevated concentrations from chlorinated tap water. For the volatile THMs, approximately equal contributions to total exposure come from four areas: ingestion of drinking-water, inhalation of indoor air largely due to volatilization from drinking-water, inhalation and dermal exposure during showering or bathing, and ingestion of food, with all but food exposure arising primarily from drinking-water. Indoor air exposure to the volatile THMs is particularly important in countries with low rates of ventilation in houses and high rates of showering and bathing.

Guideline values	
Chloroform	0.3 mg/litre
Bromoform	0.1 mg/litre
Dibromochloromethane (DBCM)	0.1 mg/litre
Bromodichloromethane (BDCM)	0.06 mg/litre
Occurrence	THMs are not expected to be found in raw water (unless near a pollution source) but are usually present in finished or chlorinated water; concentrations are generally below 100 µg/litre. In most circumstances, chloroform is the dominant compound.

TDIs	
Chloroform	15 µg/kg of body weight, derived from the lower 95% confidence limit for the 5% incidence of hepatic cysts, generated by PBPK modelling, in beagle dogs that ingested chloroform in toothpaste for 7.5 years, using an uncertainty factor of 25 (10 for intraspecies differences in toxicokinetics and toxicodynamics and 2.5 for differences in interspecies toxicodynamics)
Bromoform	17.9 µg/kg of body weight, based on the absence of histopathological lesions in the liver in a well conducted and well documented 90-day study in rats, using an uncertainty factor of 1000 (100 for intra- and interspecies variation and 10 for possible carcinogenicity and short duration of exposure)
DBCM	21.4 µg/kg of body weight, based on the absence of histopathological effects in the liver in a well conducted and well documented 90-day study in rats, using an uncertainty factor of 1000 (100 for intra- and interspecies variation and 10 for the short duration of the study); an additional uncertainty factor for potential carcinogenicity was not applied because of the questions regarding mouse liver tumours from corn oil vehicles and inconclusive evidence of genotoxicity
Basis of guideline derivation for BDCM	Application of the linearized multistage model for the observed increases in incidence of kidney tumours in male mice observed in an NTP bioassay, as these tumours yield the most protective value
Limit of detection	0.1–0.2 µg/litre (method detection limits) by purge-and-trap and liquid–liquid extraction and direct aqueous injection in combination with a chromatographic system; 0.1 µg/litre by GC with ECD; 2.2 µg/litre by GC/MS
Treatment achievability	Concentrations of chloroform, bromoform, BDCM and DBCM in drinking-water are generally below 0.05 mg/litre. Concentrations can be reduced by changes to disinfection practice (e.g., reducing organic THM precursors) or using air stripping.
Guideline derivation	
• allocation to water	20% of TDI for bromoform and DBCM 75% of TDI for chloroform
• weight	60-kg adult
• consumption	2 litres/day
Additional comments on THMs	For authorities wishing to establish a total THM standard to account for additive toxicity, the following fractionation approach could be taken: $\frac{C_{bromoform}}{GV_{bromoform}} + \frac{C_{DBCM}}{GV_{DBCM}} + \frac{C_{BDCM}}{GV_{BDCM}} + \frac{C_{chloroform}}{GV_{chloroform}} \leq 1$ where C = concentration and GV = guideline value. It is emphasized that adequate disinfection should never be compromised in attempting to meet guidelines for THMs. Nevertheless, in view of the potential link between adverse reproductive outcomes and THMs, particularly brominated THMs, it is recommended that THM levels in drinking-water be kept as low as practicable.

Additional comments on chloroform	• In countries with low rates of ventilation in houses and high rates of showering and bathing, the guideline value could be lowered to account for the additional exposures from inhalation of indoor air largely due to volatilization from drinking-water and inhalation and dermal exposure during showering or bathing. • The guideline value is based on the same study as in the third edition; the increase in value is primarily a result of an increase in the allocation of exposure in drinking-water from 50% to 75% to account for the fact that chloroform is used less now than it was in 1993 when the original guideline was developed.
Additional comments on BDCM	• Although a health-based value of 21 µg/litre is derived, the previous guideline of 60 µg/litre has been retained for two reasons: 1) both calculations were based on the same study, the only differences being the model and model assumptions used to derive the guideline value; there is therefore no scientific basis on which to justify a change in the guideline value; and 2) BDCM concentrations below 50 µg/litre may be difficult to achieve using currently available technology without compromising the effectiveness of disinfection. • As with chloroform, countries with low rates of ventilation and high rates of showering and bathing may wish to lower the guideline value to account for dermal and inhalation exposures, although, as noted above, concentrations below 50 µg/litre may be difficult to achieve using currently available technology without compromising the effectiveness of disinfection.

Toxicological review

Chloroform

The weight of evidence for genotoxicity of chloroform is considered negative. IARC has classified chloroform as possibly carcinogenic to humans (Group 2B) based on limited evidence of carcinogenicity in humans but sufficient evidence of carcinogenicity in experimental animals. The weight of evidence for liver tumours in mice is consistent with a threshold mechanism of induction. Although it is plausible that kidney tumours in rats may similarly be associated with a threshold mechanism, there are some limitations of the database in this regard. The most universally observed toxic effect of chloroform is damage to the centrilobular region of the liver. The severity of these effects per unit dose administered depends on the species, vehicle and method by which the chloroform is administered.

Bromoform

In an NTP bioassay, bromoform induced a small increase in relatively rare tumours of the large intestine in rats of both sexes but did not induce tumours in mice. Data from a variety of assays on the genotoxicity of bromoform are equivocal. IARC has classified bromoform in Group 3 (not classifiable as to its carcinogenicity to humans).

Dibromochloromethane

In an NTP bioassay, DBCM induced hepatic tumours in female and possibly in male mice but not in rats. The genotoxicity of DBCM has been studied in a number of assays, but the available data are considered inconclusive. IARC has classified DBCM in Group 3 (not classifiable as to its carcinogenicity to humans).

Bromodichloromethane

IARC has classified BDCM in Group 2B (possibly carcinogenic to humans). BDCM gave both positive and negative results in a variety of *in vitro* and *in vivo* genotoxicity assays. In an NTP bioassay, BDCM induced renal adenomas and adenocarcinomas in both sexes of rats and male mice, rare tumours of the large intestine (adenomatous polyps and adenocarcinomas) in both sexes of rats and hepatocellular adenomas and adenocarcinomas in female mice. Exposure to BDCM has also been linked to a possible increase in reproductive effects (increased risk for spontaneous abortion or stillbirth).

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to THMs. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline values for THMs other than chloroform were recommended after a detailed evaluation of the compounds. A health-based guideline value of 0.03 mg/litre was established for chloroform only, as few data existed for the remaining THMs and, for most water supplies, chloroform was the most commonly encountered member of the group. It was noted that the guideline value for chloroform was obtained using a linear multistage extrapolation of data obtained from male rats, a mathematical model that involves considerable uncertainty. It was also mentioned that although the available toxicological data were useful in establishing a guideline value for chloroform only, the concentrations of the other THMs should also be minimized. Limits ranging from 0.025 to 0.25 mg/litre, which represent a balance between the levels that can be achieved given certain circumstances and those that are desirable, have been set in several countries for the sum of bromoform, DBCM, BDCM and chloroform. In the second edition of the Guidelines, published in 1993, no guideline value was set for total THMs, but guideline values were established separately for all four THMs. Authorities wishing to establish a total THM standard to account for additive toxicity could use a fractionation approach in which the sum of the ratios of each of the four THMs to their respective guideline values is less than or equal to 1. The 1993 Guidelines established health-based guideline values of 0.1 mg/litre for both bromoform and DBCM, and guideline values of 0.06 mg/litre for BDCM and 0.2 mg/litre for chloroform, associated with an upper-bound excess lifetime cancer risk of 10^{-5}, were derived. The guideline value of 0.2 mg/litre for chloroform was retained in the addendum to the second edition of the Guidelines, published

in 1998, but was developed on the basis of a TDI for threshold effects. These guideline values were brought forward to the third edition.

Assessment date

The risk assessment was conducted in 2004.

Principal references

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12.122 Uranium

Uranium is widespread in nature, occurring in granites and various other mineral deposits. Uranium is used mainly as fuel in nuclear power stations. Uranium 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. Intake of uranium through air is low, and it appears that intake through food is between 1 and 4 µg/day. Intake through drinking-water is normally extremely low; however, in circumstances in which uranium is present in a drinking-water source, the majority of intake can be through drinking-water.

Provisional guideline value	0.015 mg/litre The guideline value is designated as provisional because of outstanding uncertainties regarding the toxicology and epidemiology of uranium as well as difficulties concerning its technical achievability in smaller supplies.
Occurrence	Levels in drinking-water are generally less than 1 µg/litre, although concentrations as high as 700 µg/litre have been measured in private supplies.

TDI	0.6 µg/kg of body weight per day, based on the application of an uncertainty factor of 100 (for inter- and intraspecies variation) to a LOAEL (equivalent to 60 µg of uranium per kg of body weight per day) for degenerative lesions in the proximal convoluted tubule of the kidney in male rats in a 91-day study in which uranyl nitrate hexahydrate was administered in drinking-water. It was considered unnecessary to apply an additional uncertainty factor for the use of a LOAEL instead of a NOAEL and the short length of the study because of the minimal degree of severity of the lesions and the short half-life of uranium in the kidney, with no indication that the severity of the renal lesions will be exacerbated following continued exposure. This is supported by data from epidemiological studies.
Limit of detection	0.01 µg/litre by ICP/MS; 0.1 µg/litre by solid fluorimetry with either laser excitation or UV light; 0.2 µg/litre by ICP using adsorption with chelating resin
Treatment achievability	1 µg/litre should be achievable using conventional treatment, e.g., coagulation or ion exchange
Guideline derivation • allocation to water • weight • consumption	 80% of TDI (because intake from other sources is low in most areas) 60-kg adult 2 litres/day
Additional comments	• The data on intake from food in most areas suggest that intake from food is low and support the higher allocation to drinking-water. In some regions, exposure from sources such as soil may be higher and should be taken into account in setting national or local standards. • The concentration of uranium in drinking-water associated with the onset of measurable tubular dysfunction remains uncertain, as does the clinical significance of the observed changes at low exposure levels. A guideline value of up to 30 µg/litre may be protective of kidney toxicity because of uncertainty regarding the clinical significance of changes observed in epidemiological studies. • Only chemical, not radiological, aspects of uranium toxicity have been addressed here. • A document on depleted uranium, which is a by-product of natural uranium, is available.

Toxicological review

There are insufficient data regarding the carcinogenicity of uranium in humans and experimental animals. Nephritis is the primary chemically induced effect of uranium in humans. Little information is available on the chronic health effects of exposure to environmental uranium in humans. A number of epidemiological studies of populations exposed to uranium in drinking-water have shown a correlation with alkaline phosphatase and β-microglobulin in urine along with modest alterations in proximal tubular function. However, the actual measurements were still within the normal physiological range.

History of guideline development

The 1958 and 1963 WHO *International Standards for Drinking-water* did not refer to uranium. The 1971 International Standards stated that uranium should be controlled in drinking-water, but that insufficient information was available to enable a tentative limit to be established. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, it was concluded that no action was required for uranium. A health-based guideline value for uranium was not derived in the 1993 Guidelines, as adequate short- and long-term studies on the chemical toxicity of uranium were not available. Until such information became available, it was recommended that the limits for radiological characteristics of uranium be used. The equivalent for natural uranium, based on these limits, is approximately 0.14 mg/litre. In the addendum to the Guidelines, published in 1998, a health-based guideline value of 0.002 mg/litre was established. This guideline value was designated as provisional, because it may be difficult to achieve in areas with high natural uranium levels with the treatment technology available and because of limitations in the key study. It was noted that several human studies are under way that may provide helpful additional data.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Uranium in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/118).

12.123 Vinyl chloride

Vinyl chloride is used primarily for the production of PVC. Owing to its high volatility, vinyl chloride has rarely been detected in surface waters, except in contaminated areas. Unplasticized PVC is increasingly being used in some countries for water mains supplies. Migration of vinyl chloride monomer from unplasticized PVC is a possible source of vinyl chloride in drinking-water. It appears that inhalation is the most important route of vinyl chloride intake, although drinking-water may contribute a substantial portion of daily intake where PVC piping with a high residual content of vinyl chloride monomer is used in the distribution network. Vinyl chloride has been reported in groundwater as a degradation product of the chlorinated solvents trichloroethene and tetrachloroethene.

Guideline value	0.0003 mg/litre (0.3 µg/litre)
Occurrence	Rarely detected in surface waters, the concentrations measured generally not exceeding 10 µg/litre; much higher concentrations found in groundwater and well water in contaminated areas; concentrations up to 10 µg/litre detected in drinking-water
Basis for guideline derivation	Application of a linear extrapolation by drawing a straight line between the dose, determined using a pharmocokinetic model, resulting in tumours in 10% of animals in rat bioassays involving oral exposure and the origin (zero dose), determining the value associated with the upper-bound risk of 10^{-5} and assuming a doubling of the risk for exposure from birth
Limit of detection	0.01 µg/litre by GC with ECD or FID with MS for confirmation
Treatment achievability	0.001 mg/litre should be achievable using air stripping
Additional comments	• The results of the linear extrapolation are nearly identical to those derived using the linearized multistage model. • As vinyl chloride is a known human carcinogen, exposure to this compound should be avoided as far as practicable, and levels should be kept as low as technically feasible. • Vinyl chloride is primarily of concern as a potential contaminant from some grades of PVC pipe and is best controlled by specification of material quality.

Toxicological review

There is sufficient evidence of the carcinogenicity of vinyl chloride in humans from industrial populations exposed to high concentrations via the inhalation route, and IARC has classified vinyl chloride in Group 1. Studies of workers employed in the vinyl chloride industry have shown a marked exposure–response for all liver cancers, angiosarcomas and hepatocellular carcinoma, but no strong relationship between cumulative vinyl chloride exposure and other cancers. Animal data show vinyl chloride to be a multisite carcinogen. When administered orally or by inhalation to mice, rats and hamsters, it produced tumours in the mammary gland, lungs, Zymbal gland and skin, as well as angiosarcomas of the liver and other sites. Evidence indicates that vinyl chloride metabolites are genotoxic, interacting directly with DNA. DNA adducts formed by the reaction of DNA with a vinyl chloride metabolite have also been identified. Occupational exposure has resulted in chromosomal aberrations, micronuclei and sister chromatid exchanges; response levels were correlated with exposure levels.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* did not refer to vinyl chloride. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, no guideline value was recommended, because the occurrence of vinyl chloride in water seemed to be associated primarily with the use of poorly polymerized PVC water pipes, a problem that was more appropriately controlled by product specification. The 1993 Guidelines calculated a guideline value of

0.005 mg/litre for vinyl chloride based on an upper-bound excess lifetime cancer risk of 10^{-5}.

Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (1999) *Vinyl chloride*. Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 215).

WHO (2003) *Vinyl chloride in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/119).

12.124 Xylenes

Xylenes are used in blending petrol, as a solvent and as a chemical intermediate. They are released to the environment largely via air. Exposure to xylenes is mainly from air, and exposure is increased by smoking.

Guideline value	0.5 mg/litre
Occurrence	Concentrations of up to 8 µg/litre have been reported in surface water, groundwater and drinking-water; levels of a few milligrams per litre were found in groundwater polluted by point emissions. Xylenes can also penetrate plastic pipe from contaminated soil.
TDI	179 µg/kg of body weight, based on a NOAEL of 250 mg/kg of body weight per day for decreased body weight in a 103- week gavage study in rats, correcting for 5 days per week dosing and using an uncertainty factor of 1000 (100 for inter- and intraspecies variation and 10 for the limited toxicological end-points)
Limit of detection	0.1 µg/litre by GC/MS; 1 µg/litre by GC with FID
Treatment achievability	0.005 mg/litre should be achievable using GAC or air stripping
Guideline derivation • allocation to water • weight • consumption	 10% of TDI 60-kg adult 2 litres/day
Additional comments	The guideline value exceeds the lowest reported odour threshold for xylenes in drinking-water.

Toxicological review

Xylenes are rapidly absorbed by inhalation. Data on oral exposure are lacking. Xylenes are rapidly distributed in the body, predominantly in adipose tissue. They are almost completely metabolized and excreted in urine. The acute oral toxicity of xylenes is low. No convincing evidence for teratogenicity has been found. Long-term carcino-

genicity studies have shown no evidence for carcinogenicity. *In vitro* as well as *in vivo* mutagenicity tests have proved negative.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to xylenes. The 1993 Guidelines proposed a health-based guideline value of 0.5 mg/litre for xylenes, noting that this value exceeds the lowest reported odour threshold for xylenes in drinking-water (0.02 mg/litre).

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Xylenes in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/25).

12.125 Zinc

Zinc is an essential trace element found in virtually all food and potable water in the form of salts or organic complexes. The diet is normally the principal source of zinc. Although levels of zinc in surface water and groundwater normally do not exceed 0.01 and 0.05 mg/litre, respectively, concentrations in tap water can be much higher as a result of dissolution of zinc from pipes.

In 1982, JECFA proposed a PMTDI for zinc of 1 mg/kg of body weight. The daily requirement for adult men is 15–20 mg/day. It was considered that, taking into account recent studies on humans, the derivation of a guideline value is not required at this time. However, drinking-water containing zinc at levels above 3 mg/litre may not be acceptable to consumers (see chapter 10).

History of guideline development

The 1958 WHO *International Standards for Drinking-water* suggested that concentrations of zinc greater than 15 mg/litre would markedly impair the potability of the water. The 1963 and 1971 International Standards retained this value as a maximum allowable or permissible concentration. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 5.0 mg/litre was established for zinc, based on taste considerations. The 1993 Guidelines concluded that, taking into account recent studies on humans, the derivation of a guideline value was not required at this time. However, drinking-water containing zinc at levels above 3 mg/litre may not be acceptable to consumers.

Assessment date

The risk assessment was originally conducted in 1993. The Final Task Force Meeting in 2003 agreed that this risk assessment be brought forward to this edition of the *Guidelines for Drinking-water Quality*.

Principal reference

WHO (2003) *Zinc in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/17).

ANNEX 1

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[1] In chapter 11, selected bibliographical references are included at the end of each microbial fact sheet. In chapter 12, principal references are provided at the end of each chemical fact sheet.

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ANNEX 2

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10. *Workshop on Drinking-water Quality Surveillance and Safety, Nadi, Fiji, 29 October–1 November 2001*
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    - *vii. Polynuclear aromatic hydrocarbons*
    - *viii. Cyanazine*
    - *ix. 1,2-Dichloropropane (1,2-DCP)*
    - *x. Pentachlorophenol*
    - *xi. Terbuthylazine (TBA)*
    - *xii. Trihalomethanes*

xiii. *1,1,1-Trichloroethane*
xiv. *1,2-Dibromoethane*
xv. *1,2-Dichloroethane*
xvi. *Di(2-ethylhexyl)adipate*
xvii. *2-Phenylphenol*
xviii. *2,4-Dichlorophenoxyacetic acid*
xix. *Acrylamide*
xx. *Aldicarb*
xxi. *Aldrin and Dieldrin*
xxii. *Antimony*
xxiii. *Arsenic*
xxiv. *Barium*
xxv. *Bentazone*
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xxviii. *Cadmium*
xxix. *Carbofuran*
xxx. *Carbon Tetrachloride*
xxxi. *Monochloramine*
xxxii. *Chlordane*
xxxiii. *Monochloroacetic acid*
xxxiv. *Chlorite and Chlorate*
xxxv. *Chlorpyrifos*
xxxvi. *Copper*
xxxvii. *DDT and its Derivatives*
xxxviii. *Dimethoate*
xxxix. *Diquat*
xl. *Endosulfan*
xli. *Endrin*
xlii. *Epichlorohydrin*
xliii. *Fenitrothion*
xliv. *Fluoride*
xlv. *Glyphosate and AMPA*
xlvi. *Halogenated Acetonitriles*
xlvii. *Heptachlor and Heptachlor Epoxide*
xlviii. *Hexachlorobenzene*
xlix. *Hexachlorobutadiene*
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li. *Malathion*
lii. *Manganese*
liii. *Methoxychlor*
liv. *Methyl Parathion*

lv. *Monochlorobenzene*
lvi. *MX*
lvii. *Dialkyltins*
lviii. *Parathion*
lix. *Permethrin*
lx. *Propanil*
lxi. *Pyriproxyfen*
lxii. *Sulfate*
lxiii. *Inorganic Tin*
lxiv. *Toluene*
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vii. *Nickel*
viii. *Trichloroethene*
ix. *Trihalomethanes*
x. *1,4-Dioxane*
xi. *MTBE*
xii. *Petroleum oils*
xiii. *Permethrin*
xiv. *Chlorite and chlorate*

ANNEX 3

Annex 3 has been deleted in the first addendum to the Third Edition

ANNEX 4

Chemical summary tables

Table A4.1 Chemicals excluded from guideline value derivation

Chemical	Reason for exclusion
Amitraz	Degrades rapidly in the environment and is not expected to occur at measurable concentrations in drinking-water supplies
Beryllium	Unlikely to occur in drinking-water
Chlorobenzilate	Unlikely to occur in drinking-water
Chlorothalonil	Unlikely to occur in drinking-water
Cypermethrin	Unlikely to occur in drinking-water
Deltamethrin	Unlikely to occur in drinking-water
Diazinon	Unlikely to occur in drinking-water
Dinoseb	Unlikely to occur in drinking-water
Ethylene thiourea	Unlikely to occur in drinking-water
Fenamiphos	Unlikely to occur in drinking-water
Formothion	Unlikely to occur in drinking-water
Hexachlorocyclohexanes (mixed isomers)	Unlikely to occur in drinking-water
MCPB	Unlikely to occur in drinking-water
Methamidophos	Unlikely to occur in drinking-water
Methomyl	Unlikely to occur in drinking-water
Mirex	Unlikely to occur in drinking-water
Monocrotophos	Has been withdrawn from use in many countries and is unlikely to occur in drinking-water
Oxamyl	Unlikely to occur in drinking-water
Phorate	Unlikely to occur in drinking-water
Propoxur	Unlikely to occur in drinking-water
Pyridate	Not persistent and only rarely found in drinking-water
Quintozene	Unlikely to occur in drinking-water
Toxaphene	Unlikely to occur in drinking-water
Triazophos	Unlikely to occur in drinking-water
Tributyltin oxide	Unlikely to occur in drinking-water
Trichlorfon	Unlikely to occur in drinking-water

Table A4.2 Chemicals for which guideline values have not been established

Chemical	Reason for not establishing a guideline value
Aluminium	Owing to limitations in the animal data as a model for humans and the uncertainty surrounding the human data, a health-based guideline value cannot be derived; however, practicable levels based on optimization of the coagulation process in drinking-water plants using aluminium-based coagulants are derived: 0.1 mg/litre or less in large water treatment facilities, and 0.2 mg/litre or less in small facilities
Ammonia	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Asbestos	No consistent evidence that ingested asbestos is hazardous to health
Bentazone	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Bromochloroacetate	Available data inadequate to permit derivation of health-based guideline value
Bromochloroacetonitrile	Available data inadequate to permit derivation of health-based guideline value
Chloral hydrate (trichloroacetaldehyde)	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Chloride	Not of health concern at levels found in drinking-water[a]
Chlorine dioxide	Guideline value not established because of the rapid breakdown of chlorine dioxide and because the chlorite provisional guideline value is adequately protective for potential toxicity from chlorine dioxide
Chloroacetones	Available data inadequate to permit derivation of health-based guideline values for any of the chloroacetones
Chlorophenol, 2-	Available data inadequate to permit derivation of health-based guideline value
Chloropicrin	Available data inadequate to permit derivation of health-based guideline value
Dialkyltins	Available data inadequate to permit derivation of health-based guideline values for any of the dialkyltins
Dibromoacetate	Available data inadequate to permit derivation of health-based guideline value
Dichloramine	Available data inadequate to permit derivation of health-based guideline value
Dichlorobenzene, 1,3-	Toxicological data are insufficient to permit derivation of health-based guideline value
Dichloroethane, 1,1-	Very limited database on toxicity and carcinogenicity
Dichloroethene, 1,1-	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Dichlorophenol, 2,4-	Available data inadequate to permit derivation of health-based guideline value
Dichloropropane, 1,3-	Data insufficient to permit derivation of health-based guideline value
Di(2-ethylhexyl)adipate	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Diquat	Rarely found in drinking-water, but may be used as an aquatic herbicide for the control of free-floating and submerged aquatic weeds in ponds, lakes and irrigation ditches
Endosulfan	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Fenitrothion	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Fluoranthene	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Formaldehyde	Occurs in drinking-water at concentrations well below those at which toxic effects may occur

Glyphosate and AMPA	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Hardness	Not of health concern at levels found in drinking-water[a]
Heptachlor and heptachlor epoxide	Occurs in drinking-water at concentrations well below those at which toxic effects may occur

continued

Table A4.2 ***Continued***

Chemical	Reason for not establishing a guideline value
Hexachlorobenzene	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Hydrogen sulfide	Not of health concern at levels found in drinking-water[a]
Inorganic tin	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Iodine	Available data inadequate to permit derivation of health-based guideline value, and lifetime exposure to iodine through water disinfection is unlikely
Iron	Not of health concern at concentrations normally observed in drinking-water, and taste and appearance of water are affected below the health-based value
Malathion	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Methyl parathion	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Methyl *tertiary*-butyl ether (MTBE)	Any guideline that would be derived would be significantly higher than concentrations at which MTBE would be detected by odour
Monobromoacetate	Available data inadequate to permit derivation of health-based guideline value
Monochlorobenzene	Occurs in drinking-water at concentrations well below those at which toxic effects may occur, and health-based value would far exceed lowest reported taste and odour threshold
MX	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Parathion	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Permethrin	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Petroleum products	Taste and odour will in most cases be detectable at concentrations below those concentrations of concern for health, particularly with short-term exposure
pH	Not of health concern at levels found in drinking-water[b]
Phenylphenol, 2- and its sodium salt	Occurs in drinking-water at concentrations well below those at which toxic effects may occur
Propanil	Readily transformed into metabolites that are more toxic; a guideline value for the parent compound is considered inappropriate, and there are inadequate data to enable the derivation of guideline values for the metabolites
Silver	Available data inadequate to permit derivation of health-based guideline value
Sodium	Not of health concern at levels found in drinking-water[a]
Sulfate	Not of health concern at levels found in drinking-water[a]
Total dissolved solids (TDS)	Not of health concern at levels found in drinking-water[a]
Trichloramine	Available data inadequate to permit derivation of health-based guideline value
Trichloroacetonitrile	Available data inadequate to permit derivation of health-based guideline value
Trichlorobenzenes (total)	Occurs in drinking-water at concentrations well below those at which toxic effects may occur, and health-based value would exceed lowest reported odour threshold
Trichloroethane, 1,1,1-	Occurs in drinking-water at concentrations well below those at which toxic effects may occur

Zinc	Not of health concern at concentrations normally observed in drinking-water[a]

[a] May affect acceptability of drinking-water (see chapter 10).
[b] An important operational water quality parameter.

Table A4.3 Guideline values for chemicals that are of health significance in drinking-water

Chemical	Guideline value[a] (mg/litre)	Remarks
Acrylamide	0.0005[b]	
Alachlor	0.02[b]	
Aldicarb	0.01	Applies to aldicarb sulfoxide and aldicarb sulfone
Aldrin and dieldrin	0.00003	For combined aldrin plus dieldrin
Antimony	0.02	
Arsenic	0.01 (P)	
Atrazine	0.002	
Barium	0.7	
Benzene	0.01[b]	
Benzo[*a*]pyrene	0.0007[b]	
Boron	0.5 (T)	
Bromate	0.01[b] (A, T)	
Bromodichloromethane	0.06[b]	
Bromoform	0.1	
Cadmium	0.003	
Carbofuran	0.007	
Carbon tetrachloride	0.004	
Chlorate	0.7 (D)	
Chlordane	0.0002	
Chlorine	5 (C)	For effective disinfection, there should be a residual concentration of free chlorine of ≥0.5 mg/litre after at least 30 min contact time at pH <8.0
Chlorite	0.7 (D)	
Chloroform	0.3	
Chlorotoluron	0.03	
Chlorpyrifos	0.03	
Chromium	0.05 (P)	For total chromium
Copper	2	Staining of laundry and sanitary ware may occur below guideline value
Cyanazine	0.0006	
Cyanide	0.07	
Cyanogen chloride	0.07	For cyanide as total cyanogenic compounds
2,4-D (2,4-dichlorophenoxyacetic acid)	0.03	Applies to free acid
2,4-DB	0.09	
DDT and metabolites	0.001	
Di(2-ethylhexyl)phthalate	0.008	
Dibromoacetonitrile	0.07	
Dibromochloromethane	0.1	
1,2-Dibromo-3-chloropropane	0.001[b]	
1,2-Dibromoethane	0.0004[b] (P)	
Dichloroacetate	0.05[b] (T, D)	
Dichloroacetonitrile	0.02 (P)	
Dichlorobenzene, 1,2-	1 (C)	

continued

Table A4.3 ***Continued***

Chemical	Guideline value (mg/litre)	Remarks
Dichlorobenzene, 1,4-	0.3 (C)	
Dichloroethane, 1,2-	0.03[b]	
Dichloroethene, 1,2-	0.05	
Dichloromethane	0.02	
1,2-Dichloropropane (1,2-DCP)	0.04 (P)	
1,3-Dichloropropene	0.02[b]	
Dichlorprop	0.1	
Dimethoate	0.006	
Dioxane, 1,4-	0.05[b]	
Edetic acid (EDTA)	0.6	Applies to the free acid
Endrin	0.0006	
Epichlorohydrin	0.0004 (P)	
Ethylbenzene	0.3 (C)	
Fenoprop	0.009	
Fluoride	1.5	Volume of water consumed and intake from other sources should be considered when setting national standards
Hexachlorobutadiene	0.0006	
Isoproturon	0.009	
Lead	0.01	
Lindane	0.002	
Manganese	0.4 (C)	
MCPA	0.002	
Mecoprop	0.01	
Mercury	0.006	For inorganic mercury
Methoxychlor	0.02	
Metolachlor	0.01	
Microcystin-LR	0.001 (P)	For total microcystin-LR (free plus cell-bound)
Molinate	0.006	
Molybdenum	0.07	
Monochloramine	3	
Monochloroacetate	0.02	
Nickel	0.07	
Nitrate (as NO_3^-)	50	Short-term exposure
Nitrilotriacetic acid (NTA)	0.2	
Nitrite (as NO_2^-)	3	Short-term exposure
	0.2 (P)	Long-term exposure
Pendimethalin	0.02	
Pentachlorophenol	0.009[b] (P)	
Permethrin	0.3	Only when used as a larvicide for public health purposes
Pyriproxyfen	0.3	
Selenium	0.01	
Simazine	0.002	
Styrene	0.02 (C)	
2,4,5-T	0.009	
Terbuthylazine	0.007	
Tetrachloroethene	0.04	
Toluene	0.7 (C)	

Table A4.3 ***Continued***

Chemical	Guideline value (mg/litre)	Remarks
Trichloroacetate	0.2	
Trichloroethene	0.02 (P)	
Trichlorophenol, 2,4,6-	0.2[b] (C)	
Trifluralin	0.02	
Trihalomethanes		The sum of the ratio of the concentration of each to its respective guideline value should not exceed 1
Uranium	0.015 (P, T)	Only chemical aspects of uranium addressed
Vinyl chloride	0.0003[b]	
Xylenes	0.5 (C)	

[a] P = provisional guideline value, as there is evidence of a hazard, but the available information on health effects is limited; T = provisional guideline value because calculated guideline value is below the level that can be achieved through practical treatment methods, source protection, etc.; A = provisional guideline value because calculated guideline value is below the achievable quantification level; D = provisional guideline value because disinfection is likely to result in the guideline value being exceeded; C = concentrations of the substance at or below the health-based guideline value may affect the appearance, taste or odour of the water, leading to consumer complaints.

[b] For substances that are considered to be carcinogenic, the guideline value is the concentration in drinking-water associated with an upper-bound 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 upper-bound estimated excess lifetime cancer risks of 10^{-4} and 10^{-6} can be calculated by multiplying and dividing, respectively, the guideline value by 10.

"Note: This index has not been updated. It does not reflect any new entries or changes that result from the incorporation of the first addendum into the third edition of the Guidelines for Drinking-water Quality."

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Page numbers in **bold** indicate main discussions.