WATER QUALITY AND STANDARDS

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Summary

Water is an essential material for all organisms on earth to sustain life, and a satisfactory water supply must be made available to consumers. It is required that drinking water not be contaminated by microbes or chemical substances harmful to human health. Pathogenic bacteria, viruses and protozoa in drinking water cause waterborne infectious diseases. The pollution source, pathogenicity, and characteristics of the main microbes that damage human health are described individually. Regarding chemical pollutions, chemical contaminants may be naturally occurring, industrial or agricultural use chemicals that cause adverse health effects in humans. The chemical pollution source, characteristics and effects on humans are described individually. Water quality guidelines and standards of drinking water are necessary to prevent damage to humans by waterborne pathogens and chemicals.

WHO drinking-water guidelines values such as heavy metals, inorganics, organics (i.e. Volatile organic compounds (VOC), pesticides) and radionuclides are described. The water used for comfortable human life also requires water quality guidelines and standards in relation to human health. Furthermore, water quality guidelines are needed for industrial, agricultural, aquacultural and emergency usage. However, a suitable aquatic environment is required in order to protect aquatic organisms. Outlines of these water quality guidelines and standards are presented.

1. Introduction

Water is essential for all of the organisms on earth to sustain life, and a satisfactory water supply must be made available to consumers. Thus every effort should be made to achieve a water quality as high as practicable. Protection of water supplies from contamination is the first line of defense. Water of higher quality may be required for some special purposes, such as renal dialysis, cleaning of contact lens, or for certain purposes in food production. There may also be special requirements for those who are significantly immuno-compromised.

Access to safe water for human health and environment is a basic human right and an essential component of effective policy for health and environmental protection. The importance of water, sanitation and hygiene for development are international political concerns. In some regions, investments in water supply and sanitation for health yield a net economic benefit, since the reductions in adverse effects and health care costs outweigh the costs of undertaking the intervention. Drinking-water quality is a serious concern for health in countries at all levels of development. The standards are derived to take account of the needs of an individual through a normal lifetime. Those at greatest risk of waterborne disease are infants and young children, people who are debilitated or living under unhygienic conditions and the elderly.

The judgment of safety - or what is an acceptable level of risk in particular circumstances - is a matter in which society as a whole has a role to play. The final judgment as to whether the benefit resulting from the adoption of any of the guideline values as national or local standards justifies the cost is for each country to decide. What must be emphasized is that the guidelines be adaptable to take account of socio-cultural, economic and environmental conditions of the settings in which they are applied. The nature and form of drinking-water standards may vary among countries and regions. There is no single approach that is universally applicable. It is essential in the development and implementation of standards that the current and planned legislation relating to the water, health and local government is taken into account and that the capacity of potential regulators in the country is assessed. Approaches that may have worked in one country or region do not necessarily transfer to other countries or regions. It is essential that each country review its needs and capacities in developing a regulatory framework.

The community has a right to water of appropriate quality, but also adequate quantity. Adequate quantity of water for basic hygiene is a pre-requisite for health protection and improving access to safe drinking-water can result in tangible health improvements. A holistic risk management approach to drinking-water supply increases confidence in the safety of drinking-water and reduces reliance on end-point testing. These plans systematically assess risks throughout a drinking-water supply, from the catchments, aquifer and its source water, through to the consumer's tap, and identify the ways that these risks can be managed including methods to ensure that barriers and control measures are working effectively. A risk management plan assesses the integrity of the entire water supply system and is able to incorporate strategies to deal with day-to-day management of water quality, including the inevitable upsets and failures.

Source protection is almost invariably the best method of ensuring safe drinking-water and is to be preferred to treating a contaminated water supply to render it suitable for consumption. Once a potentially hazardous situation has been recognized however, the risk to health, the availability of alternative sources, and the availability of suitable remedial measures must be considered so that a decision can be made about the acceptability of the supply.

In this chapter, parts of health-related water quality, water contamination and standards are referring the contents of WHO Guidelines for drinking water quality 3rd edition.Furthermore, the water used for comfortable human life requires the water quality guidelines and standards in relation to human health. For instance, the same level as drinking-water quality standards is required as for bath water where the water touches the skin directly. As for the swimming water, it is necessary to disinfect using chlorine or ozone and the same water quality of drinking-water is required. Additionally, the miscellaneous use water, such as artificial fountains and the air-conditioning cooling water, etc. should also maintain these water qualities individually.

On the other hand, some water quality levels or standards are individually necessary for the water used for the industrial activities. In agriculture that takes part in the production of food, the water quality guidelines and standards that do not influence for the harvests of field rice and vegetables are necessary for agricultural water, such as irrigation water. As for water of aquaculture, it is important to maintain a suitable water quality for the stable and increased production. For the cultivation of fish and shellfish, the standards and guidelines are also needed. The water used in industry and manufacturing might be exhausted of harmful microorganisms and chemicals. Scale and corrosion often occur in industrial use water depending on the quality of the water. Thus, some water quality standards for wastewater discharge are needed in consideration of the influence to human health and the environment.

2. Health-related Water Quality

The great majority of health-related water quality problems are the result of microbial (bacteriological viral, protozoal or other biological) contamination. Nevertheless, an appreciable number of serious health concerns may occur as a result of the chemical contamination of drinking-water.

2.1. Microbial Aspects

Microbial water quality may vary rapidly and over a wide range. Short-term peaks in pathogen occurrence may increase disease risks considerably and may also trigger outbreaks of waterborne disease. Therefore reliance cannot be placed on water quality measurements, even when made frequently, to determine the microbial safety of drinking-water. End-product testing is an important quality-control or verification procedure to ensure water quality. If adequate protection and effective treatment of drinking-water throughout the distribution system are not provided, the community will be exposed to the risk of outbreaks of intestinal and other infectious diseases. In general, the greatest microbial risks are associated with ingestion of feces-contaminated water. Fecal waste is a largest source of pathogenic bacteria, viruses, protozoa and helminthes.

Escherichia coli provide conclusive evidence of fecal pollution. However, the absence of *E. coli* will not necessarily indicate freedom from these organisms, since some viruses and protozoa are more resistant to disinfection. In addition to fecally borne pathogens, other hazardous organisms, e.g. guinea worm, cyanobacteria and *Legionella* may be important for public health under specific circumstances.

Disinfection is unquestionably important in supplying safe water. The destruction of microbial pathogens is essential and very commonly carried out by using reactive chemical agents such as chlorine. Disinfection is an effective barrier to many pathogens in drinking-water and is widely used for surface waters and for groundwater subjected to fecal contamination. Residual disinfection is used to provide a partial safeguard against low level contamination and re-growth in water. However, chlorine disinfection has limitations against the protozoan pathogens such as *Cryptosporidium* and some viruses. An overall management strategy is essential to be implemented where multiple processes are used in conjunction with disinfection to prevent or remove microbial contamination.

It should be however mentioned the formation of chemical by-products by use of chemical disinfectants in water treatment, although the risks to health from these by-products are extremely small in comparison with the risks of water-born infections. It is important that disinfection should not be compromised in attempting to control such by-products.

Drinking-water is still a major contributor to the community burden of enteric disease in many parts of the world, because available water sources are fecally contaminated. Therefore, improvement of drinking-water quality appreciably reduces the overall risks of enteric disease transmission. Therefore, as a first step in the application of health based targets to achieve safe drinking-water supply, a community can set as their health target a quantifiable reduction in the overall level of diarrheal disease. Such a reduction could be reached, for example, by the implementation of a water treatment at the household or community level (by disinfection and related processes) capable of achieving a significant reduction of pathogen loads in the water. The use of an epidemiological approach to directly measure the achievement of a health risk target is a powerful tool to demonstrate the achievement of safer drinking-water. In many situations this can be an effective first incremental step in the eventual goal of achieving increasingly safer drinking-water. Where the overall burden of enteric disease is low, the possible effects of water quality interventions are less easily measured by epidemiological studies. In order to relate the effects of improved drinking-water quality to health risks in the population, risk assessment models can be constructed as an alternative. Such models take into account the raw water quality, treatment effects, water quality changes during distribution and/or storage and drinking-water consumption to provide an estimate of consumer exposure to contaminants.

By combining these exposure data with dose-response models, a risk estimate can be provided. Risk managers will then have to decide on the acceptability of the risk. Decisions about risk acceptance are highly complex and need to take account of different dimensions of risk. In addition to the probability and severity of an effect, there are important socio-cultural, economic, environmental and political dimensions that play an important role in decision-making. Negotiations play an important role in these processes, and the outcome may very well be unique in each situation. Notwithstanding the complexity of decisions about risk, there is a need for a baseline definition of tolerable risk for the development of guidelines and as a departure point for decisions in specific situations. For the purpose of guideline derivation, the preferred option is to define an absolute upper level of tolerable public health risk, which is the same for exposure to each individual hazard. Descriptions of the level of risk in relation to water are usually expressed in terms of specific health outcomes (such as cancer, diarrheal disease, et cetera). Given the diverse range of water-related infections and the severity of immediate and delayed health outcomes with some infections, a common exchange unit is essential in order to account for acute, delayed and chronic effects (including both morbidity and mortality). These include diverse effects; varied severity weightings; and acute versus delayed effects such as adverse birth outcomes, cancer, cholera, dysentery, infectious hepatitis, intestinal worms, skeletal fluorosis, typhoid, association of Guillain-Barré syndrome with campylobacteriosis, (mild self-limiting diarrhea through to significant case mortality rates). This variety of health impacts also causes difficulties for making transparent decisions based on cost-effectiveness considerations, or when a particular intervention reduces the probability of one type of disease (e.g. infectious disease) but at the same time increases the probability of another illness (e.g. cancer).

2.2. Chemical Aspects

The health risk due to toxic chemicals in drinking-water differs from that caused by microbial contaminants. The problems associated with chemical constituents in water arise primarily from their ability to cause adverse health effects after prolonged periods of exposure. There are few chemical constituents in water that can lead to health problems resulting from a single exposure, and short-term exposure is not likely to lead to health impairment. Only a few chemicals are of immediate health concern in any given circumstance, although numerous chemicals may occur in drinking-water.

Exposure to high levels of naturally occurring fluoride can lead to mottling of teeth and, in severe cases, crippling skeletal fluorosis. Similarly, arsenic may occur naturally, and excess exposure to arsenic in drinking-water may result in a significant cancer risk. Other naturally-occurring chemicals of health concern include uranium and selenium.

The presence of nitrate and nitrite in water, causing methaemoglobinaemia in infants, may result from the excessive application of fertilizers or from leaching of wastewater or other organic wastes into surface water and groundwater.

In areas with aggressive or acidic waters, the use of lead pipes and fittings or solder can result in elevated lead levels in drinking-water, which may cause adverse neurological effects in children.

Some health effects may occur as a result of specific chemical deficiencies in the diet, of which water forms a part. Important examples are ophthalmic goiter caused by iodine deficiency and dental caries resulting from low fluoride intake. No attempt has been made in the Guidelines to define a minimum desirable concentration of such substances in drinking-water because it is assumed that the diet would usually be the principal source of beneficial substances.

2.3. Radiological Aspects

The radiological health risk should be arisen from the presence of naturally occurring radionuclides in water and it should be considered as part of overall system assessment, although the contribution of drinking-water to total exposure to radionuclides is very small under normal circumstances.

2.4. Acceptability Aspects

In assessing the quality of drinking-water, consumers rely principally upon their senses. Microbial, chemical and physical water constituents may affect the appearance, odor, or taste of the water, and the consumer will evaluate the quality and acceptability of the water on the basis of these criteria. Water that is highly turbid, is highly colored, or has an objectionable taste or odor may be regarded by consumers as unsafe and may be rejected for drinking purposes. In extreme cases, consumers may avoid aesthetically unacceptable but otherwise safe supplies in favor of more pleasant but potentially unsafe sources of drinking-water.

Although the standards are based on the best available public health evidence, there is no guarantee that consumers will be satisfied or dissatisfied by water supplies to meet these standards. It is therefore wise to be aware of consumer perceptions and to take into account both health-related standards and aesthetic criteria when assessing drinking-water supplies.

3. Water Contaminants

3.1. Microbial Aspects

Waterborne infectious diseases are caused by pathogenic bacteria, viruses and protozoa in drinking-water. Contamination of pathogens may also trigger outbreaks of waterborne disease and may produce large numbers of patients in the limited area independently from age, sex, etc. Thus, much attention has been paid to drinking-water as a cause of outbreaks of gastric infectious disease.

Table 1 demonstrates the human pathogens that are known be transmitted by drinking-water consumption. Most of the pathogens are distributed worldwide, but some outbreaks are regional. The effects of exposure to pathogens depend on populations and may lead to different health effects in different populations. Sensitive subgroups in the population such groups as the young, the elder, and the pregnant women. All of infected individuals will not develop symptomatic disease. The ratio of symptomatic carriers differs for pathogens and population characteristics. Infected carriers may contribute to secondary spread of pathogens by transmitting pathogens in water.

Pathogen	Health effect	Persistence in water*	Resistance to chlorine
Bacteria			
Burkholderia pseudomallei	Low	May multiply	Low
Campylobacter jejuni, C. coli	High	Moderate	Low
Escherichia coli -pathogenic	High	Moderate	Low
E.coli-enterohaemorrhagic	High	Moderate	Low
Legionella spp.	Multiply	Multiply	Low
Non-tuberculous mycobacteria	Low	Multiply	High
Pseudomonas aeruginosa[e]	Moderate	May multiply	Moderate
Salmonella typhi	High	Moderate	Low
Other salmonellae	High	May multiply	Low
Shigella spp.	High	Short	Low
Vibrio cholerae	High	Short	Low
Yersinia enterocolitica	High	Long	Low
Viruses			
Adenoviruses	High	Long	Moderate
Enteroviruses	High	Long	Moderate
Hepatitis A & E	High	Long	Moderate
Norwalkvirus and Sapoviruses	High	Long	Moderate
Rotavirus	High	Long	Moderate
Protozoa			
Acanthamoeba spp.	High	Long	High
Cryptosporidium parvum	High	Long	High
Cyclospora cayetanensis	High	Long	High
Entamoeba histolytica	High	Moderate	High
Giardia intestinalis	High	Moderate	High
Naegleria fowleri	High	May multiply	High
Toxoplasma gondii	High	Long	High
<u>Helminthes</u>			
Dracunculus medinensis	High	Moderate	Moderate
Schistosoma spp.	High	Short	Moderate

*: Detection period for infective stage in water at 20C:short up to1 week; moderate , 1 week to 1 month; long, over 1 month. WHO drinking water quality guidelines (2004)

Table 1: Orally transmitted waterborne pathogens

Some of the pathogens in contaminated drinking-water lead to severe and sometimes life-threatening diseases such as typhoid, cholera, and, diseases caused by *E. coli* O157. Others produce less severe outcomes such as diarrheal disease (examples rotavirus, *Cryptosporidium*) to healthy adults. Some pathogens transmitted by drinking-water cause disease opportunistically in subjects with impaired immunity. They are able to cause disease in people with impaired defense mechanisms, such as the elderly or the very young, patients with burns or extensive wounds, those undergoing immunosuppressive therapy, or those with acquired immunodeficiency syndrome (AIDS).

The pathogens may be transmitted through various routes to drinking-water. Drinking-water is one of the major vehicles for pathogens transmitted by the fecal-oral route, contaminated food, hands, utensils and clothing also play a role in the transmission. Pathogenic agents in water have several properties different from chemical pollutants. Pathogens often adhere to suspended solids in water, and an infective dose cannot be predicted from their average concentration in water. Pathogens multiply in their host, thereby increasing the chances of infection. Unlike many chemical agents, the dose response of pathogens is not cumulative.

Certain serious illnesses result from inhalation of water droplets (aerosols) in which the causative organisms have multiplied because of warm temperatures and the presence of nutrients. These include Legionellosis (*Legionella* spp.) and those caused by the amoebae *Naegleria fowleri* (primary amoebic meningoencephalitis) and *Acanthamoeba* spp. (amoebic meningitis, pulmonary infections).

Other pathogens transmitted by drinking-water cause have as their primary route of infection contact or inhalation, rather than by ingestion. Such pathogens maybe naturally present in the environment. Water used by such patients for drinking or bathing, if it contains large numbers of these organisms, can produce various infections of the skin and the mucous membranes of the eye, ear, nose, and throat.

Most organisms do not grow in water, but are able to persist in drinking-water. After leaving the host, pathogens gradually lose viability and the ability to infect. Pathogens with low persistence are be spread by person-to-person contact rather than by drinking-water. Persistence is affected by several factors, and temperature is the most important. Persistence is decreasing as increasing temperature of water and ultraviolet radiation in sunlight may affect persistence. Viruses are unable to multiply in water.

3.1.1. Bacterial Pathogens of Fecal Origin

a) Aeromonas

Aeromonas have readily been isolated from sewage, all types of natural waters and even from chlorinated drinking-waters. Some causal relationship exists between the presence of *Aeromonas* spp. in drinking-water and cases of human diarrhea. *Aeromonas* species are members of the family Vibrionaceae and six species of the mesophilic aeromonads are accepted as pathogens in humans, namely: *A. hydrophila, A. caviae*, *A. veronii subsp sobria, A. jandaei, A. veronii subsp veronii* and *A. schubertii*. The pathogens are involved in human infections, such as gastroenteritis, peritonitis, endocarditis, meningitis, septicemia, wounds, respiratory as well as urinary tract infections.

b) *Bacillus*

Bacillus spores are found in many foods, especially rice, pulses vegetables, tap water, and bottled water, and cause opportunistic infections as well as gastrointestinal diseases. *Bacillus* spp. are Gram-positive, strictly aerobic and form heat-resistant endospores. *Bacillus* spp. are divided into four subgroups: 1) *B. polymyxa*; 2) *B. subtilis,* which includes *B. cereus* and *B. licheniformis*; 3) *B. brevis* and 4) *B. anthracis*. Several *Bacillus* spp. are pathogenic for humans and animals. *Bacillus cereus* causes food poisoning (similar to staphylococcal food-poisoning), the commonest association being with reheated cooked rice and pulses. *Bacillus anthracis* is the causative agent of anthrax in humans and animals. 35% of gastrointestinal illness was attributed to the consumption of drinking-water meeting current water quality guidelines.

c) Campylobacter

Numerous waterborne outbreaks of campylobacteriosis have been reported worldwide, which are introduced into water by contamination with the faeces of wild birds. Campylobacters are one of the most important causes of acute gastroenteritis worldwide. *Campylobacter jejuni* is the most important human pathogen, and induces infection as few as 1 000 organisms. Clinical symptoms are crampy abdominal pain, diarrhea, chills and fever. The species occur in a variety of environments, but all appear to be inhabitants of the gastrointestinal tract of wild and domestic animals including household pets. The occurrence in surface waters is strongly dependant on rainfall, water temperature and the presence of waterfowl.

d) Escherichia coli pathogenic strains

Escherichia coli is the species most commonly isolated from human faecal samples and is part of the normal intestinal flora of healthy individuals. Generally, *E. coli* bacteria are not associated with adverse health effects. *Escherichia coli* O157:H7 and other enterotoxigenic or enteropathogenic *E. coli* cause non-bloody diarrhea, hemorrhagic colitis and/or hemolytic uremic syndrome. Waterborne transmission of pathogenic *E. coli* has been well documented and reported from both recreational waters and contaminated drinking-water.

e) Helicobacter

Helicobacter pylori is one of the most common organisms causing infections such as acute and chronic gastritis which may effect around half of the worlds population. There are at least 14 species of *Helicobacter* associated with different hosts. *Helicobacter pylori* were found in surface and groundwater and the survival capacity of these organisms in surface water was found to be up to 20-30 days. The majority of infections with *H. pylori* occur in children. The infections are more prevalent in developing countries and are associated with overcrowded living conditions.

f) Legionella

Legionellae are ubiquitous in the environment and can proliferate at the higher temperatures experienced at times in piped distribution systems and more commonly in hot and warm water systems supplied with drinking-water. Exposure from drinking-water is preventable through the implementation of basic water quality management measures in buildings and/or through the maintenance of disinfection residuals throughout the piped distribution system. Legionellae are Gram-negative, rod-shaped, non-spore-forming bacteria that require L-cysteine for growth and primary isolation. *Legionella* spp. are heterotrophic bacteria found in domestic water sources and cause a lung infections resembling pneumonia. The first outbreak in Philadelphia was induced by the air-conditioning system. The low nutrient content and total bacterial count in cooling tower systems may favor the occurrence of *Legionella*. Bacteria containing aerosols penetrate the lungs and are retained by the alveoli. Legionellosis outbreaks have been attributed to contaminated potable water, cooling towers or components of water distribution systems all over the world.

g) Mycobacterium avium complex

Mycobacterium avium complex (MAC) causes human and animal infections of the lungs, lymph nodes, skin, bones, and the gastrointestinal and genitourinary tracts. MAC is heterotrophic bacteria and multiplies in suitable water environments, notably biofilms. High numbers may occur in distribution systems after events that dislodge biofilms, such as flushing or flow reversals. They are exceptionally resistant to treatment and disinfection and have been detected in 54% of ice and 35% of public drinking-water samples. Their presence in drinking-water supplies confirms this as one route of exposure.

h) Pseudomonas

Pseudomonas aeruginosa is an opportunistic pathogen, found in faeces, soil, water and sewage and multiplies in aquatic environment. *Pseudomonas aeruginosa* cause mild and trivial diseases in healthy individuals, and causes secondary infections of burn wounds, nosocomial pneumonia, nosocomial urinary tract infections and surgical wound infections. Waterborne infections are associated with warm, moist environments (i.e. indoor swimming pools and spas). Diseases result in skin rashes and pustules or outer ear canal infections.

i) Salmonella

Salmonella is hardy organisms that can survive in moist environments and in the frozen state for several months. Human infections with salmonellae are most commonly caused by ingestion of food, water or milk contaminated by human or animal excreta, or transmitted from person-to-person via fecally contaminated food and water. Most waterborne outbreaks have been associated with *S. typhi*. Symptoms of gastroenteritis appear 4 to 5 days after infection.

j) Shigella

Members of the genus *Shigella* are pathogens that cause serious disease known as bacillary dysentery. As few as 200 organisms could cause disease if ingested, and fever and watery diarrhea occur early in the disease. The most severe illness are caused by *Shigella dysenteriae* type 1, which produces Shiga toxin. Shigellae are harbored by humans and transferred from person-to-person by the faecal-oral route. Due to the severity of diseases caused by *Shigella* bacteria, it is of extreme public health importance to reduce the risk of waterborne outbreaks. Of the enteric bacterial pathogens, shigellae seem to be the best adapted to cause human disease. Epidemics of shigellosis occur in crowded communities where human carriers exist. *Shigella* can be spread by flies, fingers, food or faeces.

k) Staphylococcus

Staphylococcus aureus is an aerobic and gram-positive coccus, and causes a broad range of serious infections throughout the body such as diarrhea, fever, abdominal cramps, electrolyte imbalance and loss of fluids. *Staphylococcus aureus* is found in the external environment and in the nasopharynx of 20% to 40% of adults. Such carriers provide the reservoir for the spread of staphylococcal infections, most frequently by way of the hands. Food handlers or persons who have staphylococcal lesions on the skin are the most likely to contaminate food and water destined for consumption.

l) Vibrio

Vibrio cholerae is a small gram-negative organism and grouped according to its O-antigen. Symptoms of cholera resulted from heat-labile cholera enterotoxin are an increase in peristalses followed by loose, watery and mucus-flecked "rice-water" stools (patient may lose as much as 10 liters of liquid per day) and death results in as many as 60% of untreated patients as a result of severe dehydration and loss of electrolytes. Pathogenic *Vibrio* species are associated with mollusks and crustaceans found in freshwater lakes, rivers and marine environments in temperate and/or tropical regions throughout the world. Cholera, the disease caused by *V. cholerae*, is spread as a faecal-oral disease and people acquire the infection by the ingestion of fecally contaminated water and food. *Vibrio cholerae* is extremely sensitive to disinfection processes and outbreaks of *V. cholerae* can be prevented by boiling practices and chlorine disinfection of drinking-water.

m) Yersinia

The genus *Yersinia* is classified in the family Enterobacteriaceae and comprises seven species. *Yersinia* spp. are gram-negative rods that are motile at 25C but not at 37C.

Yersinia enterocolitica penetrates cells of the intestinal mucosa, causing ulcerations of the terminal ilium. Yersiniosis generally presents as an acute gastroenteritis with diarrhea, fever and abdominal pain. Pathogenic *Y. enterocolitica* has been detected in sewage and polluted surface water. However, *Y. enterocolitica* strains detected in drinking-water are more commonly non-pathogenic strains of probable environmental origin. *Yersinia* spp. is transmitted by the faecal-oral route, with the major source of infection considered to be foods. Ingestion of contaminated water is also a potential source of infection

n) Cyanobacteria

Public health concern regarding cyanobacteria (commonly called blue-green algae) relates to the ability of many species and strains of these organisms to produce cyanotoxins which are toxic when ingested. These toxins pose a challenge for management. Unlike most toxic chemicals, high concentrations of cyanotoxins rarely occur dissolved in the water as these toxins are usually contained within cyanobacterial cells. Exposure to high concentrations usually results from ingestion of accumulated cell material. In contrast to pathogenic bacteria, these cells do not proliferate within the human body after uptake, only in the aquatic environment before intake.

3.1.2. Viral Pathogens of Fecal Origin

a) Adenoviruses

Adenoviruses are widespread in nature infecting birds, mammals and amphibians. Human adenoviruses cause infections of the gastro-intestinal tract, eyes, respiratory tract and various sub-clinical infections. The presence of adenoviruses has been confirmed in a variety of water environments. The only waterborne outbreaks of adenoviral diseases have been associated with swimming pools causing pharyngitis and conjunctivitis. The potential health risks are widely recognized, and the viruses are one of only four viruses included in the "Candidate Contaminant List" (CCL) of the Environmental Protection Agency in the USA, which is based on their potential health implications and data which indicate that they occur in large numbers in water environments.

b) Astroviruses

Astroviruses cause gastroenteritis, predominantly diarrhea, mainly in children under five years of age, and more than 80% of children between 5 and 10 years have antibodies against astroviruses. Occasional outbreaks have been reported in schools, nurseries and families. Astroviruses are present in sewage and sewage-polluted water, and the faecal-oral route is the predominant mode of transmission for astroviruses. Astrovirus-associated gastroenteritis has been associated with the consumption of contaminated food and water. Person-to-person spread is seen in nurseries, pediatric wards, families, homes for elderly and military camps.

c) Enteroviruses

Enteroviruses are among the most important viral pathogens of humans and may cause an estimated 30 million infections in the US each year. The diseases range from a mild febrile illness to myocarditis, meningoencephalitis, poliomyelitis and neonatal multi-organ failure. Enteroviruses are stable in the environment, resistant to chlorine and UV disinfection treatment, resulting in the presence in raw and treated drinking- water. Enteroviruses have world-wide distribution. Infection can be acquired through contaminated water, food or vomitus. Humans are the only known reservoirs of enteroviral infections. Children younger than 5 years of age are the most susceptible to infection, due in part to a lack of prior immunity and to poor hygienic habits.

d) Hepatitis A virus

Hepatitis A virus is a non-enveloped, positive-sense single-stranded RNA virus with an icosahedral symmetry and a diameter of 27 nm. The incubation period of hepatitis A (HA) ranges from 10 to 50 days and is usually a mild disease characterized by a sudden onset of fever, dark urine, malaise, nausea, and anorexia. Hepatitis A virus is a major source of morbidity associated with fecally contaminated food and water world wide, and readily inactivated by UV irradiation and a free-residual chlorine (2.0-2.5 mgl^{-1}).

e) Hepatitis E virus

The clinical illness of Hepatitis E virus resembles to acute viral hepatitis caused by hepatitis A virus. The incubation period of hepatitis E is 1 to 8 weeks and occurs mainly in the young adult population. Hepatitis E outbreaks are usually associated with fecally contaminated drinking-water supply systems. Notable epidemics, associated with contaminated water, have occurred in New Delhi, India (1955-56), Soviet Union (1955-56), Nepal (1973-74), Myanmar (1976-77), Kashmir, India (1978-82), China (1986-88) and Kanpur, India (1991).

f) Rotaviruses

Human rotaviruses (HRVs) are the most common cause of acute viral gastroenteritis in infants and young children. The incubation period is estimated to be less than 48 hours and symptoms include fever, vomiting, chronic watery non-bloody diarrhea and abdominal pain. In developing countries 18 million infants are infected and 800 000 die due to rotavirus infection each year. Human rotaviruses are contaminated in water and food, and are transmitted via the faecal-oral route. The first documented waterborne outbreak occurred in Colorado, USA in 1981.

3.1.3. Protozoan Pathogens of Faecal Origin

a) Acanthamoeba

Acanthamoeba are free-living in the environment, and *A. castellanii, A. polyphaga,* and *A. culbertsoni* are known to be human pathogens. *Acanthamoeba* will develop into a dormant cyst under unfavourable conditions such as temperature (-20 C to 56 C), disinfection and desiccation. *A. culbertsoni* causes granulomatous amoebic encephalitis (GAE) which is a multifocal, hemorrhagic, and necrotizing encephalitis. It is a rare but usually fatal disease. *Acanthamoeba* are found in soil, fresh and salt water. Infective cysts can be transmitted in dust and aerosols. *Acanthamoeba* keratitis outbreaks occurred due to soft contact lenses being washed with contaminated tap water. *Acanthamoeba* is associated with any fresh or salty aquatic environment, including chlorinated swimming pools, drinking-water and wells. *Acanthamoeba* cysts are resistant to chlorine, but efficiently removed by filtration processes.

b) Cryptosporidium

Cryptosporidium is an obligate, intracellular, coccidian protozoan parasite, which produces environmentally resistant oocysts (4 μm to 6 μm in diameter). These oocysts are excreted in the faeces of infected individuals. *Cryptosporidium parvum* infects the intestinal epithelia of humans and animals causing severe, life-threatening diarrhea in immuno-compromised individuals. *Cryptosporidium* oocysts are resistant to chlorine and most other disinfectants, like iodine and bromine, at concentrations used for drinking-water treatment. More than half (56%) of the waterborne cryptosporidiosis outbreaks between 1984 and 1999 were associated with drinking-water. In 1993, an outbreak of cryptosporidiosis in Milwaukee produced diarrheal illness of 403 000 persons. Rapid and effective monitoring procedures are needed at drinking-water facilities to improve public health risks.

c) *Cyclospora*

Cyclospora cayetanensis is a single cell, obligate, intracellular, coccidian protozoan parasite, and produces resistant oocysts (8 µm to 10 µm in diameter), which are excreted in the faeces of infected individuals. The *C. cayetanensis* oocysts are exceptionally resistant to disinfection and have been detected in chlorinated drinking-water. *Cyclospora cayetanensis* penetrates the small intestine of susceptible humans after ingestion of sporulated oocysts, and causes watery diarrhea, abdominal cramping, weight loss, anorexia, and myalgia. Contaminated drinking-water, irrigation water and irrigated crops are potential sources for cyclosporiasis. *Cyclospora* outbreaks have been associated with the consumption of contaminated drinking-water. The first outbreak occurred in 1990 at Chicago hospital, and the second in 12 of 14 British soldiers. *Cyclospora* oocysts have been isolated from wastewater, which is used as drinking-water sources.

d) Giardia

Giardia intestinales is responsible for the most human and mammal infections, and is flagellated protozoa which parasitize the intestines of humans and animals. *Giardia* produces trophozoites as well as environmentally resistant cysts. Symptoms of giardiasis may include diarrhea and abdominal cramps. *Giardia* can multiply in several host animal species, including humans, which excrete cysts into the environment. *Giardia* cysts survive in chlorine used for water purification systems. Drinking-water, recreational water, food and person-to-person contact have been reported to play a role in the transmission of this parasite. The waterborne transmission of *Giardia* and its outbreaks have been reported worldwide. Outbreaks have been associated with unfiltered surface water systems in which chlorination was the only treatment.

e) Microsporidium

Microsporidia are among the smallest eukaryotes and are obligate intercellular protozoan parasites. Human *Microsporidia* pathogens appear to have animal reservoirs such as pigs. Microsporidiosis is more common in immuno-compromised individuals, and is ocular or encephalitic infections but rarely diarrhea. *Microsporidia* enter individuals via ingestion or inhalation. Spores are excreted in faeces and urine and survive up to 4 months in water causing waterborne outbreaks. In the summer of 1995, *Microsporidia* were identified as the causative agent in a waterborne outbreak in Lyon, France. These organisms have been listed in the top 10 on the United States Environmental Protection Agency’s (USEPA) pathogens priority list.

f) Toxoplasma

Toxoplasma is an obligate intracellular parasite, produces resistant oocysts in the intestine of cats. Toxoplasmosis is the result of ingestion of oocysts, from cat faeces, unwashed foods, or hands after handling pet cats, contaminated soil etc., or bradyzoites in raw or undercooked meat. Few outbreaks of toxoplasmosis have been reported with drinking-water. One outbreak occurred in Canada in 1995 by drinking-water reservoir and/or its feeder streams being contaminated by faeces from wild and/or domestic cats, and in Rio de Janeiro State, Brazil, 1997-1999. Filtration and coagulation-sedimentation processes are effective to remove the chlorine-resistant oocysts.

3.1.4. Helminths

a) 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 *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. The only route of exposure is the consumption of drinking-water containing Cyclops spp. Carrying infectious *Dracunculus* larvae. The onset of symptoms occurs just prior to the local eruption of the worm. The early manifestations of urticaria, erythema, dyspnoes, vomiting, pruritus and giddiness are of an allergic nature. In about 50% of cases, whole worm is extruded in a few weeks.

3.2. Chemical Aspects

A number of chemical contaminants cause adverse health effects in humans as a consequence of prolonged exposure. Chemical contaminants in water may be categorized in various ways; however, the most appropriate is to consider the primary source of the contaminant i.e. to group chemicals according to where control may be effectively exercised. This aids in the development of approaches that are designed to prevent or minimize contamination, rather than those that rely primarily on the measurement of contaminant levels in final waters. Sources of chemicals in water related to health are therefore divided into six major source groups (see Table 2). Some contaminants may fall into more than one category and the categories are not always clear-cut. The group of naturally occurring contaminants includes many of the inorganic chemicals that are found in drinking-water as a consequence of release from rocks and soils by rainfall, some of which may become problematical only where there is environmental disturbance such as in mining areas.

Source of chemical constituents	**Examples of sources**
1) Naturally occurring	Rocks, soils etc.
2) Industry and human settlements	Mining, industries, sewage, solid wastes, urban runoff, fuel leakages
3) Agricultural activities	Manures, fertilizers, and pesticides
4) Water treatment systems	Coagulants, disinfection by-products, and piping materials
5) Larvicides used in water	Larvaecides
6) Cyanobacteria	Eutrophic lakes

Table 2: Categorization of source of chemical constituents

3.2.1. Naturally Occurring Chemicals

Chemical	**Reason for exclusion**	**Remarks**
Chloride	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water
Hardness	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water
Hydrogen sulfide	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water
PH	Not of health concern at levels found in drinking-water	An important operational water quality parameter
Sodium	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water
Sulfate	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water
Total dissolved solids (TDS)	Not of health concern at levels found in drinking-water	May affect acceptability of drinking-water

WHO drinking water quality guidelines (2004)

Table 3: Naturally occurring chemicals for which guideline values have not been established

Chemical	Guideline value[a] (mg L^{-1})	Remarks
Arsenic	0.01 (P)	
Barium	0.7	
Boron	0.5 (T)	
Chromium	0.05 (P)	For total chromium
Fluoride	1.5	Volume of water consumed and intake from other sources should be considered when setting national standards
Manganese	0.4	C[b]
Molybdenum	0.07	
Selenium	0.01	
Uranium	0.015 (P, T)	Only chemical aspects of uranium addressed

[a] Abbreviations used for provisional guideline values are as follows: P = evidence of a potential hazard but the available information on health effects is limited; T = calculated guideline value is below the level that can be achieved through practical treatment methods, source protection, etc.
[b] C = concentrations of the substance at or below the health-based guideline value may affect the appearance, taste or odour of the water, resulting in consumer complaints.
WHO drinking water quality guidelines (2004)

Table 4: Guideline values for naturally occurring chemicals those are of health significance in drinking-water

All natural water contains a range of inorganic and organic chemicals. The former derive from the rocks and soil through which water percolates or over which it flows.

The latter derive from the breakdown of plant material or from algae and other microorganisms that grow in the water or on sediments. Health-related naturally occurring compounds in drinking water are shown in Table 3 and 4.

a) 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 from 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.

Levels in natural waters generally vary between 1 and 2 μg L^{-1}, although concentrations may be elevated (up to 12 mg L^{-1}) in areas containing natural sources.

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 L^{-1} and the practical difficulties in removing arsenic from drinking-water, a guideline value of 10 μg L^{-1} is retained. In view of the scientific uncertainties, the guideline value is designated as provisional.

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 remains considerable uncertainty and controversy over both the mechanism of carcinogenicity and the shape of the dose–response curves 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.

b) 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, but 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.

Concentrations in drinking-water are generally below 100 μg L^{-1}, although concentrations above 1 mg L^{-1} have been measured in drinking-water derived from groundwater.

7.3 mg L^{-1} 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 L^{-1} and one whose water contained a concentration of 0.1 mg L^{-1}.

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.

c) 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. 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.

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 L^{-1}. 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 tumor incidence. A TDI of 0.16 mg $kg^{-1}$of body weight was calculated, based on a NOAEL of 9.6 mg kg^{-1} 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 intra-species variation)

d) 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. Total chromium concentrations in drinking-water are usually less than 2 μg L^{-1}, although concentrations as high as 120 μg L^{-1} have been reported. In a long-term carcinogenicity study in rats given chromium (III) by the oral route, no increase in tumor 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.

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 analyzing for the hexavalent form only.

e) Fluoride

Fluoride accounts for about 0.3 g kg^{-1} 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 aluminum 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. In groundwater, concentrations vary with the type of rock the water flows through but do not usually exceed 10 mg L^{-1}; the highest natural level reported is 2800 mg L^{-1}.

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 L^{-1} of drinking-water; the minimum concentration of fluoride in drinking-water required to produce it is approximately 0.5 mg L^{-1}. 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 L^{-1}, 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^{-1} and suggestive evidence of an increased risk of effects on the skeleton at total fluoride intakes above about 6 mg day^{-1}. Epidemiological evidence exists 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.

f) 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. , It has been used around 1995s 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.

Levels in fresh water typically range from 1 to 200 μg L^{-1}, although levels as high as 10 mg L^{-1} in acidic groundwater have been reported.

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. A TDI of 0.06 mg kg^{-1} of body weight was calculated, 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, taking into consideration the possible increased bioavailability of manganese from water

g) 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. Molybdenum is considered to be an essential element, with an estimated daily requirement of 0.1-0.3mg for adults. No data are available on the carcinogenicity of molybdenum by the oral route.

h) 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. In some areas selenium occurs at elevated levels in drinking-water and is associated with human health effects. It is therefore one of the high priority contaminants for screening in water supplies.

Levels in drinking-water vary greatly in different geographical areas but are usually much less than 0.01 mg L^{-1}.

Selenium is an essential element for humans, with a recommended daily intake of about 1 µg kg^{-1} of body weight for adults. Selenium compounds have been shown to be genotoxic *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^{-1} 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.

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^{-1} body weight showed no clinical or biochemical signs of selenium toxicity.

i) 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 3 m g day^{-1}. Occurrence in drinking-water is primarily as a consequence of natural sources. 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.

Levels in drinking-water are generally less than 1 µg L^{-1}, although concentrations as high as 700 µg L^{-1} have been measured in some private supplies and concentrations up to 100 µg L^{-1} have been observed in some small municipal supplies.

There are insufficient data regarding the carcinogenicity of uranium in humans and experimental animals. Data from high levels of exposure to uranium indicate that nephritis is the primary adverse effect 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 range.

0.6 µg kg^{-1} of body weight per day, based on the application of an uncertainty factor of

100 to a LOAEL 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 because of the minimal degree of severity of the lesions and the short half-life 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.

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