8
Chemical aspects

Most chemicals arising in drinking-water are of health concern only after extended exposure of years, rather than months. The principal exception is nitrate. Typically, changes in water quality occur progressively, except for those substances that are discharged or leach intermittently to flowing surface waters or groundwater supplies from, for example, contaminated landfill sites.

In some cases, there are groups of chemicals that arise from related sources – for example, the DBPs – and it may not be necessary to set standards for all of the substances for which there are guideline values. If chlorination is practised, the THMs, of which chloroform is the major component, are likely to be the main DBPs, together with the chlorinated acetic acids in some instances. In some cases, control of chloroform levels and, where appropriate, trichloroacetic acid levels will also provide an adequate measure of control over other chlorination by-products.

Several of the inorganic elements for which guideline values have been recommended are recognized to be essential elements in human nutrition. No attempt has been made here at this time to define a minimum desirable concentration of such substances in drinking-water.

Fact sheets for individual chemical contaminants are provided in chapter 12. For those contaminants for which a guideline value has been established, the fact sheets include a brief toxicological overview of the chemical, the basis for guideline derivation, treatment achievability and analytical limit of detection. More detailed chemical reviews are available (http://www.who.int/water_sanitation_health/dwq/guidelines/en/).

8.1 Chemical hazards in drinking-water

A number of chemical contaminants have been shown to cause adverse health effects in humans as a consequence of prolonged exposure through drinking-water. However, this is only a very small proportion of the chemicals that may reach drinking-water from various sources.

The substances considered here have been assessed for possible health effects, and guideline values have been proposed only on the basis of health concerns. Additional

consideration of the potential effects of chemical contaminants on the acceptability of drinking-water to consumers is included in chapter 10. Some substances of health concern have effects on the acceptability of drinking-water that would normally lead to rejection of the water at concentrations significantly lower than those of health concern. For such substances, health-based guideline values are needed, for instance, for use in interpreting data collected in response to consumer complaints.

The lists of chemicals addressed in these Guidelines do not imply that all of these chemicals will always be present or that other chemicals not addressed will be absent.

In section 2.3.2, it is indicated that "In developing national drinking-water standards based on these Guidelines, it will be necessary to take account of a variety of environmental, social, cultural, economic, dietary and other conditions affecting potential exposure. This may lead to national standards that differ appreciably from these Guidelines." This is particularly applicable to chemical contaminants, for which there is a long list, and setting standards for, or including, all of them in monitoring programmes is neither feasible nor desirable.

It is important that chemical contaminants be prioritized so that the most important are considered for inclusion in national standards and monitoring programmes.

The probability that any particular chemical may occur in significant concentrations in any particular setting must be assessed on a case-by-case basis. The presence of certain chemicals may already be known within a particular country, but others may be more difficult to assess.

In most countries, whether developing or industrialized, water sector professionals are likely to be aware of a number of chemicals that are present in significant concentrations in drinking-water supplies. A body of local knowledge that has been built up by practical experience over a period of time is invaluable. Hence, the presence of a limited number of chemical contaminants in drinking-water is usually already known in many countries and in many local systems. Significant problems, even crises, can occur, however, when chemicals posing high health risk are widespread but their presence is unknown because their long-term health effect is caused by chronic exposure as opposed to acute exposure. Such has been the case of arsenic in groundwater in Bangladesh and West Bengal, for example.

For some contaminants, there will be exposure from sources other than drinking-water, and this may need to be taken into account when setting standards and considering the need for standards. It may also be important when considering the need for monitoring. In some cases, drinking-water will be a minor source of exposure, and controlling levels in water will have little impact on overall exposure. In other cases, controlling a contaminant in water may be the most cost-effective way of reducing exposure. Drinking-water monitoring strategies, therefore, should not be considered in isolation from other potential routes of exposure to chemicals in the environment.

Table 8.1 Categorization of source of chemical constituents

Source of chemical constituents	Examples of sources
Naturally occurring	Rocks, soils and the effects of the geological setting and climate
Industrial sources and human dwellings	Mining (extractive industries) and manufacturing and processing industries, sewage, solid wastes, urban runoff, fuel leakages
Agricultural activities	Manures, fertilizers, intensive animal practices and pesticides
Water treatment or materials in contact with drinking-water	Coagulants, DBPs, piping materials
Pesticides used in water for public health	Larvicides used in the control of insect vectors of disease
Cyanobacteria	Eutrophic lakes

The scientific basis for each of the guideline values is summarized in chapter 12. This information is important in helping to modify guideline values to suit national requirements or in assessing the significance for health of concentrations of a contaminant that are greater than the guideline value.

Chemical contaminants in drinking-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.

In general, approaches to the management of chemical hazards in drinking-water vary between those where the source water is a significant contributor (with control effected, for example, through source water selection, pollution control, treatment or blending) and those from materials and chemicals used in the production and distribution of drinking-water (controlled by process optimization or product specification). In these Guidelines, chemicals are therefore divided into six major source groups, as shown in Table 8.1.

Categories may not always be clear-cut. The group of naturally occurring contaminants, for example, includes many 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 where there is environmental disturbance, such as in mining areas.

8.2 Derivation of chemical guideline values

The criteria used to decide whether a guideline value is established for a particular chemical constituent are as follows:

— there is credible evidence of occurrence of the chemical in drinking-water, combined with evidence of actual or potential toxicity; or

— the chemical is of significant international concern; or
— the chemical is being considered for inclusion or is included in the WHO Pesticide Evaluation Scheme (WHOPES) programme (approval programme for direct application of pesticides to drinking-water for control of insect vectors of disease).

Guideline values are derived for many chemical constituents of drinking-water. A guideline value normally represents the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption. A number of provisional guideline values have been established at concentrations that are reasonably achievable through practical treatment approaches or in analytical laboratories; in these cases, the guideline value is above the concentration that would normally represent the calculated health-based value. Guideline values are also designated as provisional when there is a high degree of uncertainty in the toxicology and health data (see also section 8.2.6).

There are two principal sources of information on health effects resulting from exposure to chemicals that can be used in deriving guideline values. The first and preferred source is studies on human populations. However, the value of such studies for many substances is limited, owing to lack of quantitative information on the concentration to which people have been exposed or on simultaneous exposure to other agents. However, for some substances, such studies are the primary basis on which guideline values are developed. The second and most frequently used source of information is toxicity studies using laboratory animals. The limitations of toxicology studies include the relatively small number of animals used and the relatively high doses administered, which create uncertainty as to the relevance of particular findings to human health. This is because there is a need to extrapolate the results from animals to humans and to the low doses to which human populations are usually exposed. In most cases, the study used to derive the guideline value is supported by a range of other studies, including human data, and these are also considered in carrying out a health risk assessment.

In order to derive a guideline value to protect human health, it is necessary to select the most suitable study or studies. Data from well conducted studies, where a clear dose–response relationship has been demonstrated, are preferred. Expert judgement was exercised in the selection of the most appropriate study from the range of information available.

8.2.1 Approaches taken

Two approaches to the derivation of guideline values are used: one for "threshold chemicals" and the other for "non-threshold chemicals" (mostly genotoxic carcinogens).

It is generally considered that the initiating event in the process of genotoxic chemical carcinogenesis is the induction of a mutation in the genetic material (DNA) of somatic cells (i.e., cells other than ova or sperm) and that there is a theoretical risk at

any level of exposure (i.e., no threshold). On the other hand, there are carcinogens that are capable of producing tumours in animals or humans without exerting a genotoxic activity, but acting through an indirect mechanism. It is generally believed that a demonstrable threshold dose exists for non-genotoxic carcinogens.

In deriving guideline values for carcinogens, consideration was given to the potential mechanism(s) by which the substance may cause cancer, in order to decide whether a threshold or non-threshold approach should be used (see sections 8.2.2 and 8.2.4).

The evaluation of the potential carcinogenicity of chemical substances is usually based on long-term animal studies. Sometimes data are available on carcinogenicity in humans, mostly from occupational exposure.

On the basis of the available evidence, the International Agency for Research on Cancer (IARC) categorizes chemical substances with respect to their potential carcinogenic risk into the following groups:

Group 1: the agent is carcinogenic to humans
Group 2A: the agent is probably carcinogenic to humans
Group 2B: the agent is possibly carcinogenic to humans
Group 3: the agent is not classifiable as to its carcinogenicity to humans
Group 4: the agent is probably not carcinogenic to humans

According to IARC, these classifications represent a first step in carcinogenic risk assessment, which leads to a second step of quantitative risk assessment where possible. In establishing guideline values for drinking-water, the IARC evaluation of carcinogenic compounds, where available, is taken into consideration.

8.2.2 Threshold chemicals

For most kinds of toxicity, it is believed that there is a dose below which no adverse effect will occur. For chemicals that give rise to such toxic effects, a tolerable daily intake (TDI) should be derived as follows, using the most sensitive end-point in the most relevant study, preferably involving administration in drinking-water:

$$\text{TDI} = (\text{NOAEL or LOAEL})/\text{UF}$$

where:

- NOAEL = no-observed-adverse-effect level
- LOAEL = lowest-observed-adverse-effect level
- UF = uncertainty factor

The guideline value (GV) is then derived from the TDI as follows:

$$\text{GV} = (\text{TDI} \times \text{bw} \times \text{P})/\text{C}$$

where:

- bw = body weight (see Annex 3)
- P = fraction of the TDI allocated to drinking-water
- C = daily drinking-water consumption (see Annex 3)

Tolerable daily intake

The TDI is an estimate of the amount of a substance in food and drinking-water, expressed on a body weight basis (mg/kg or μg/kg of body weight), that can be ingested over a lifetime without appreciable health risk.

Acceptable daily intakes (ADIs) are established for food additives and pesticide residues that occur in food for necessary technological purposes or plant protection reasons. For chemical contaminants, which usually have no intended function in drinking-water, the term "tolerable daily intake" is more appropriate than "acceptable daily intake," as it signifies permissibility rather than acceptability.

Over many years, JECFA and JMPR have developed certain principles in the derivation of ADIs. These principles have been adopted where appropriate in the derivation of TDIs used in developing guideline values for drinking-water quality.

As TDIs are regarded as representing a tolerable intake for a lifetime, they are not so precise that they cannot be exceeded for short periods of time. Short-term exposure to levels exceeding the TDI is not a cause for concern, provided the individual's intake averaged over longer periods of time does not appreciably exceed the level set. The large uncertainty factors generally involved in establishing a TDI (see below) serve to provide assurance that exposure exceeding the TDI for short periods is unlikely to have any deleterious effects upon health. However, consideration should be given to any potential acute effects that may occur if the TDI is substantially exceeded for short periods of time.

No-observed-adverse-effect level and lowest-observed-adverse-effect level

The NOAEL is defined as the highest dose or concentration of a chemical in a single study, found by experiment or observation, that causes no detectable adverse health effect. Wherever possible, the NOAEL is based on long-term studies, preferably of ingestion in drinking-water. However, NOAELs obtained from short-term studies and studies using other sources of exposure (e.g., food, air) may also be used.

If a NOAEL is not available, a LOAEL may be used, which is the lowest observed dose or concentration of a substance at which there is a detectable adverse health effect. When a LOAEL is used instead of a NOAEL, an additional uncertainty factor is normally applied (see below).

Uncertainty factors

The application of uncertainty (or safety) factors has been widely used in the derivation of ADIs and TDIs for food additives, pesticides and environmental contaminants. The derivation of these factors requires expert judgement and careful consideration of the available scientific evidence.

Table 8.2 Source of uncertainty in derivation of guideline values

Source of uncertainty	Factor
Interspecies variation (animals to humans)	1–10
Intraspecies variation (individual variations within species)	1–10
Adequacy of studies or database	1–10
Nature and severity of effect	1–10

In the derivation of guideline values, uncertainty factors are applied to the NOAEL or LOAEL for the response considered to be the most biologically significant.

In relation to exposure of the general population, the NOAEL for the critical effect in animals is normally divided by an uncertainty factor of 100. This comprises two 10-fold factors, one for interspecies differences and one for interindividual variability in humans (see Table 8.2). Extra uncertainty factors may be incorporated to allow for database deficiencies and for the severity and irreversibility of effects.

Factors lower than 10 were used, for example, for interspecies variation when humans are known to be less sensitive than the animal species studied. Inadequate studies or databases include those where a LOAEL was used instead of a NOAEL and studies considered to be shorter in duration than desirable. Situations in which the nature or severity of effect might warrant an additional uncertainty factor include studies in which the end-point was malformation of a fetus or in which the end-point determining the NOAEL was directly related to possible carcinogenicity. In the latter case, an additional uncertainty factor was usually applied for carcinogenic compounds for which the guideline value was derived using a TDI approach rather than a theoretical risk extrapolation approach.

For substances for which the uncertainty factors were greater than 1000, guideline values are designated as provisional in order to emphasize the higher level of uncertainty inherent in these values. A high uncertainty factor indicates that the guideline value may be considerably lower than the concentration at which health effects would actually occur in a real human population. Guideline values with high uncertainty are more likely to be modified as new information becomes available.

The selection and application of uncertainty factors are important in the derivation of guideline values for chemicals, as they can make a considerable difference in the values set. For contaminants for which there is sufficient confidence in the database, the guideline value was derived using a smaller uncertainty factor. For most contaminants, however, there is greater scientific uncertainty, and a relatively large uncertainty factor was used. The use of uncertainty factors enables the particular attributes of the chemical and the data available to be considered in the derivation of guideline values.

Allocation of intake

Drinking-water is not usually the sole source of human exposure to the substances for which guideline values have been set. In many cases, the intake of chemical

contaminants from drinking-water is small in comparison with that from other sources, such as food and air. Guideline values derived using the TDI approach take into account exposures from all sources by apportioning a percentage of the TDI to drinking-water. This approach ensures that total daily intake from all sources (including drinking-water containing concentrations of the substance at or near the guideline value) does not exceed the TDI.

Wherever possible, data concerning the proportion of total intake normally ingested in drinking-water (based on mean levels in food, air and drinking-water) or intakes estimated on the basis of consideration of physical and chemical properties were used in the derivation of the guideline values. Where such information was not available, an arbitrary (default) value of 10% for drinking-water was used. This default value is, in most cases, sufficient to account for additional routes of intake (i.e., inhalation and dermal absorption) of contaminants in water. In some cases, a specific discussion is made of the potential for exposure from intake through inhalation and dermal uptake in bathing and showering where there is evidence that this is likely to be significant, usually in circumstances where the allocation of the TDI to drinking-water is greater than 10%.

It is recognized that exposure from various media may vary with local circumstances. It should be emphasized, therefore, that the derived guideline values apply to a typical exposure scenario or are based on default values that may or may not be applicable for all areas. In those areas where relevant exposure data are available, authorities are encouraged to develop context-specific guideline values that are tailored to local circumstances and conditions. For example, in areas where the intake of a particular contaminant in drinking-water is known to be much greater than that from other sources (i.e., air and food), it may be appropriate to allocate a greater proportion of the TDI to drinking-water to derive a guideline value more suited to the local conditions. In addition, in cases in which guideline values are exceeded, efforts should be made to assess the contribution of other sources to total intake in order to interpret the health significance of the exceedance and to orient remedial measures to sources of exposure that are most relevant.

Significant figures

The calculated TDI is used to derive the guideline value, which is then rounded to one significant figure. In some instances, ADI values with only one significant figure set by JECFA or JMPR were used to calculate the guideline value. The guideline value was generally rounded to one significant figure to reflect the uncertainty in animal toxicity data and exposure assumptions made.

8.2.3 Alternative approaches

Alternative approaches being considered in the derivation of TDIs for threshold effects include the benchmark dose (BMD) (IPCS, 1994), categorical regression (IPCS, 1994) and chemical-specific adjustment factors (CSAF) (IPCS, 2001).