GENERAL REMARKS

In this eighty-fourth volume of the *IARC Monographs*, evaluations are made of evidence in relation to the carcinogenicity of arsenic (mostly naturally occurring) as a contaminant of drinking-water, as well as that of the water disinfectant chloramine and some chlorination by-products found in drinking-water. Some of the chlorination by-products evaluated here (chloral hydrate and di- and trichloroacetic acids) were evaluated previously (IARC, 1995). Chlorinated drinking-water and some chlorination by-products which are not re-evaluated in the present volume of the *Monographs* were previously evaluated in *IARC Monographs* Volume 52 (IARC, 1991). Those evaluations are listed in Table 1.

Table 1. Evaluations of chlorinated drinking-water, some chemicals used in the chlorination of drinking-water and some chlorination by-products, from *IARC Monographs* Volume 52 (1991)

Agent	Degree of evidence[a,b] of carcinogenicity		Overall evaluation of carcinogenicity to humans
	Human	Animal	
Chlorinated drinking-water	I	I	3
Some chemicals used in the chlorination of drinking-water			
Sodium chlorite	ND	I	3
Hypochlorite salts	ND	I	3
Chlorination by-products			
Bromodichloromethane	I	S	2B
Bromoform	I	L	3
Chlorodibromomethane	I	L	3
Halogenated acetonitriles			
Bromochloroacetonitrile	ND	I	3
Chloroacetonitrile	ND	I	3
Dibromoacetonitrile	ND	I	3
Dichloroacetonitrile	ND	I	3
Trichloroacetonitrile	ND	I	3

[a] I, inadequate evidence; S, sufficient evidence; L, limited evidence; ND, no data.
[b] For definitions of degrees of evidence and groupings of evaluations, see Preamble.
[Modified from the General Remarks to Vol. 52]

Water is essential to life, and the maintenance of an adequate supply of unpolluted water is a requirement for both human health and good environmental quality. Human demands upon the earth's water are great, and in some regions dangerously so. Water is taken for human use, irrigation and industry and is returned as industrial discharge, agricultural run-off and microbiologically contaminated, treated or untreated sewage. Water quality varies according to these discharges, the season and the geology of an area. The most critical characteristic of water for human health is its microbiology.

The microbiological quality of water can be controlled effectively by disinfection methods, which normally involve the introduction of chemical oxidants into the water supply. Chemicals used on a substantial scale as disinfectants are chlorine, hypochlorite, chloramine, chlorine dioxide and ozone. Chlorination is almost universally accepted as the method of choice for purifying water supplies. It was first used on a continuous basis for this purpose at the beginning of the twentieth century, and it is also used for sewage treatment in a few countries. Since some water suppliers have difficulty in maintaining acceptable water quality, particularly with regard to taste and odour, chlorine may be used in combination with ozone, chlorine dioxide, ammonia and activated charcoal. These treatments are sometimes followed by dechlorination, for example with sulfur dioxide.

There are substantial and irrefutable benefits of disinfection of water supplies by chemical methods, including chlorination. Any major change to these programmes would need to be evaluated fully as to its costs and benefits with regard not only to the need to maintain microbiological safety but also to the possible long-term adverse effects of alternatives to chlorination.

The investigation of possible risks for cancer from consuming chlorinated drinking-water in human populations is difficult, and hindered by a number of methodological obstacles. Chlorination may produce quite different profiles of chemical by-products in different areas. Characterization of a person's water consumption is complicated by the fact that, in many parts of the world, people change residence from time to time, and the nature of their source of domestic water changes as a consequence. Furthermore, people may consume water not only at home but also at work and elsewhere, and may drink not only chlorinated water but also unchlorinated water, bottled water, boiled water and other liquids, which will greatly influence their exposure to chlorination by-products. Exposure to constituents of water other than by ingestion — by inhalation or skin absorption — may also occur. Even if associations between human cancer risk and exposure to residential chlorinated water supplies can be demonstrated, they may be due to other constituents of the water that is chlorinated or to particular characteristics of the populations who live in areas served by such water supplies.

Evaluation of chlorinated water for carcinogenicity in experimental animals is similarly challenging. Few studies have been conducted in which the effects, if any, of constituents of chlorinated water have been compared with those of constituents of water from the same supply collected before chlorination.

Chlorination/disinfection by-products in water are formed when chlorine-based disinfectants react with the available organic matter in water. As many as 500 chlorination by-

products have been identified, including trihalomethanes (THMs), and halogenated acids and aldehydes (HAAs), some of which are carcinogenic to experimental animals. Water in which these compounds and other trace contaminants are present is a very complex mixture. Formation and occurrence of the by-products is dependent on a number of factors, including the method of disinfection, the level and content of organic matter, pH, temperature and duration of treatment. THMs and HAAs are generally the most prevalent by-products; others occur at lower levels, but current knowledge on them is limited due to the small number of studies. Little is known about how various by-products are correlated; they may differ by region due to differences in determinants of their formation. THMs have regularly been used as a marker for the mixture of by-products in water, because they are measured routinely, but little is known as to whether they are a good marker for individual by-products such as chloral hydrate, trichloroacetic acid, dichloroacetic acid and MX ('mutagen X', 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5*H*)-furanone). Only a small fraction of the chlorination by-products that have been identified in drinking-water have been tested for carcinogenicity.

Chlorinated drinking-water has been reported to be associated with the development of some human cancers, most particularly cancer of the urinary bladder. The epidemiological studies have examined exposure to chlorinated drinking-water rather than to specific disinfection by-products, and they are described in the Introduction section of the Monographs on chloramine, chloral hydrate, dichloroacetic acid, trichloroacetic acid and MX. However, they were not formally reviewed by this Working Group. It is important to recognize that none of the disinfectant by-products reviewed by IARC in this or previous volumes of the *Monographs* can be considered individually as the plausible causes for the cancers observed in human studies. When the potency of the by-products that have been evaluated is viewed in the context of their concentrations in drinking-water, it appears that these are at least three orders of magnitude too low to account for the risks implied. In most circumstances, however, the toxicity of a mixture cannot be assessed solely by evaluating individual compounds identified in this mixture. This is particularly the case for chlorinated drinking-water that contains hundreds of disinfection by-products, none of which dominates the toxicity of the mixture.

Arsenic and arsenic compounds were evaluated previously (IARC, 1980, 1987) as being *carcinogenic to humans* (Group 1) on the basis of *sufficient evidence* of an increased risk for skin cancer among patients exposed to inorganic arsenic through medical treatment, and an increased risk for lung cancer among workers involved in mining and smelting, who inhaled inorganic arsenic.

The natural and anthropogenic occurrence of arsenic in drinking-water has been increasingly recognized as a major public health concern in several regions of the world over the past several decades. Significant exposures have been documented in Argentina, Bangladesh, Chile, China, India (West Bengal), Mexico, Taiwan, China, and parts of the south-western USA. As an example, tube-wells began to be used for drinking-water in the 1970s in Bangladesh to control cholera and other gastrointestinal diseases that can be spread by drinking contaminated surface water. In the 1990s, it was discovered that the

water from many of these wells was contaminated with arsenic. Worldwide, an estimated 160 million people live in regions with naturally elevated levels of arsenic in the drinking-water, due to the presence of arsenic-rich geological formations.

In this Volume, informative epidemiological studies of the prevalence of human cancer are reviewed — mainly ecological studies in Taiwan, China, and Chile, and several case–control and cohort studies — in relation to arsenic in drinking-water, which occurs primarily as inorganic arsenic (arsenate and, to a lesser extent, arsenite). Also in this Volume, studies of the carcinogenicity in experimental animals of dimethylarsinic acid, a methylated metabolite of inorganic arsenic, are reviewed for the first time.

Substances evaluated in this Volume of *Monographs* are those for which either there is published evidence of a causal association with human cancer when present in drinking-water (arsenic) or bioassays for carcinogenicity in experimental animals have been conducted (dimethylarsenic acid, chloral hydrate, di- and trichloroacetic acid, MX and chloramine).

References

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