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PRODUCTS IN DRINKING-WATER CHLORINATION AS POTENTIAL MUTAGENS IN DRINKING-WATER

by

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TARGET 20

Water pollution

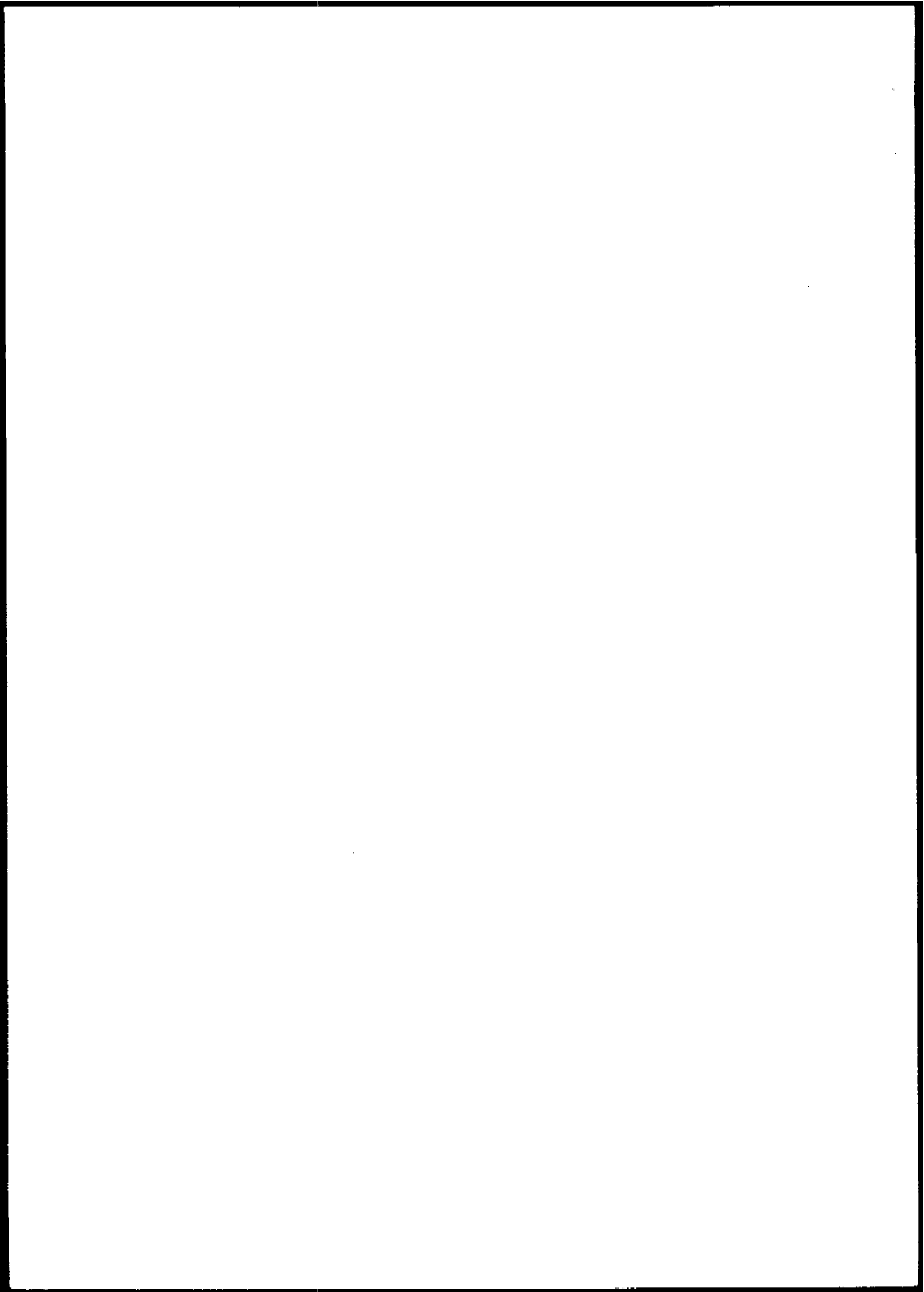
By 1990, all people of the Region should have adequate supplies of safe drinking-water, and by the year 1995 pollution of rivers, lakes and seas should no longer pose a threat to human health.

Index:

DRINKING WATER
WATER TREATMENT
MUTAGENS

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1. Introduction

In view of the still high numbers of waterborne diseases, the United Nations's General Assembly adopted Resolution 35/18 concerning the implementation of the International Drinking-Water Supply and Sanitation Decade (IDWSSD), to ensure that safe water and water hygiene, indispensable prerequisites for human health, be taken into consideration. In fulfilling this resolution, the WHO Regional Office for Europe proclaimed the Regional Target 20 as follows:

By 1990, all people of the Region should have adequate supplies of safe drinking water, and by the year 1995 pollution of rivers, lakes and seas should no longer pose a threat to human health.

Within the Region, more than 100 million people are not connected to a safe water supply system at home, and about 200 million are without adequate sewage disposal.

A dominating role is played by the diminution of infectious waterborne diseases. Diseases, such as typhoid fever, infectious hepatitis, dysentery and cholera, form an important part of all cases of infectious diseases which are subject to registration. In several Mediterranean countries, cholera occurred endemically, whereas diarrhoea is still one of the major causes for disease and death of newborn and small infants in most of the southern countries of the Region.

It is generally known that the supply of drinking water free from infectious germs (for instance, bacteria and viruses) is an indispensable prerequisite for any effective, prophylactic initiative towards combating these diseases.

On the other hand, it cannot be ignored that the quality of raw water, surface water, and to an increasing degree also groundwater, has deteriorated more and more due to anthropogenic activities. In this process, the ever-increasing number of potentially toxic substances from households, trade and industry, as well as from agriculture, play an important role.

Whereas in the past, drinking-water supplies were guaranteed mainly by high-quality groundwater, in recent years, more and more surface water of a lower quality has to be used in order to provide the drinking-water system with the required amount of water. This trend will accelerate in future years. In the German Democratic Republic, the use of surface water sources had already reached a rate of 25% in 1985 [1].

This alarming tendency of deterioration of raw-water quality indicates that for the achievement of the set target, the supply of "safe" drinking water requires enormous efforts towards the protection of the limited water capacities. At the same time, it is necessary to develop effective and inexpensive technologies for the treatment of contaminated raw water to ensure a quality acceptable for drinking purposes, i.e. water which is safe in terms of sanitation and which is up to the standards set by the WHO Guidelines for Drinking-Water Quality [2]. These activities require a joint approach by all countries in the European Region.

Among different treatment methods, disinfection occupies a key position, being indispensable in the prevention of waterborne infectious diseases.

However, since Rook and Bellar discovered that toxic by-products were formed during chlorination [3,4], this method of disinfection of drinking water is being considered in a completely new light. Investigations carried out in recent years have clearly revealed that the trihalomethanes (THM) discovered by Rook and Bellar are only the top of the "iceberg", which consists of a multitude of by-products, known and to a great extent still unknown (e.g. non-volatile halogenated hydrocarbons). With regard to the health implications of these substances, our present knowledge is still incomplete. The fact that a number of these by-products are potential mutagens and/or carcinogens has alarmed scientists and public alike.

In the following chapters, an up-to-date state-of-the-art will be given with regard to the knowledge of mutagenic/carcinogenic by-products from drinking-water chlorination, as well as a survey on alternative methods of drinking-water disinfection. At the same time, recommendations derived from the present knowledge will be presented. These recommendations will contribute to a reduction of potential hazards to humans posed by by-products from disinfection of drinking water.

2. Presence of organic substances in drinking water and their sources

Long before it was possible to identify individual substances, the presence of organic matter in drinking water was known. Only by the application of effective concentration methods, linked with computerized gas chromatography/mass spectrometry, did it become possible to characterize such substances in quantitative and qualitative terms. Since then, many single substances representing different groups of chemicals have been detected in drinking water. A great amount of literature is available. Schackelford and Keith report 1256 chemical compounds that they had detected in different waters in the United States of America [5]. Fielding and Packham published a list of 360 chemical compounds which had been found in drinking water [6], and Tardiff reported an additional 300 in American drinking water [7]. Garrison gives a survey on the frequency of occurrence of organic compounds in drinking water according to chemical classes [8] (see Table 1).

Table 1. Frequency of occurrence of chemical classes of organic compounds in drinking water [8]

Chemical Class	Proportion in %
Alcohols, aldehyde, ketone	13.9
Alkane hydrocarbons	7.0
Alkene hydrocarbons	1.0
Benzenoid hydrocarbons	7.2
Carbohydrates	0.2
Carboxylic acids	1.5
Esters, ethers, heterocyclic oxygen compounds	8.6
Halogenated compounds	47.1
Nitrogen compounds	3.6
Phenols and naphthols	1.5
Phosphorus compounds	1.0
Polynuclear aromatic hydrocarbons	5.1
Sulfur compounds	2.5

Clearly, the halogenated organic hydrocarbons head the list of organic substances in drinking water, the other substances following way behind.

Data provided by Slooff and Zoeteman on a quantitative classification of pollutants in drinking water are very interesting [9] (see Tables 2 and 3).

Table 2. Organic compounds detected in drinking water at concentrations >10 µg/litre [9]

Compounds	Detected in			Maximum concentration (µg/litre)
	USA	Netherlands	Switzerland	
Benzene	+	+	+	50
Bromoform	+	+		10
Chloroform	+	+		311
Dibromochloromethane	+	+		50
Dichlorobromomethane	+	+		72
Methylindene	+	+		19
1-methylnaphthalene	+		+	11
Trichloroethylene	+	+	+	113
Vinylchloride	+	+		10

A number of known mutagenic/carcinogenic substances occur within the selected concentration of 10 µ/litre.

Table 3. Organic compounds detected in drinking water at concentrations of 1 - 10 µg/litre [9]

Compounds	Detected in			Maximum concentration (µg/litre)
	USA	Netherlands	Switzerland	
Aldrin	+	+		5.4
bis(2-chloroisopropylether)	+	+		2.5
n-Decane	+	+	+	2.4
Dibutylphtalate	+	+	+	1.0
o-Dichlorobenzene	+	+		1.0
p-Dichlorobenzene	+	+	+	3.0
1,2-Dichloroethane	+	+		8.0
Dieldrin	+	+		8.0
Diethylphtalate	+	+		1.0
2,6-Dimethylnaphtalene		+	+	1.0
Ethylbenzene	+	+	+	2.3
Hexachloroethane	+	+		4.3
2-Methylnaphthalene	+	+	+	1.4
n-Nonane	+		+	2.4
n-Propylbenzene	+	+	+	2.4
Tetrachloromethane	+	+		3.0
n-Udecane	+		+	2.5
o-Xylene	+	+	+	4.1
m-Xylene	+	+	+	7.5

Table 3 also shows a multitude of substances hazardous to health to be found within the concentration range between 1 - 10 µg/litre. The occurrence of these organic compounds in drinking water can be explained as follows:

- contamination of raw waters
- contamination within the drinking-water distribution system
- formation of by-products during chlorination of drinking water.

Considering the amount of major halogenated hydrocarbons produced annually, it is not surprising to find them in drinking water (see Table 4).

Table 4. Quantity of important halogenated hydrocarbons produced in 1973 [10]

<u>Compound</u>	World production in tons (1973)
Ethylene dichloride	19 500 000
Vinylchloride	10 500 000
Perchloroethylene	1 050 000
Trichloroethylene	1 010 000
Carbon tetrachloride	1 000 000
Dichlorofluoromethane	570 000
Trichlorofluoromethane	485 000
Methylene chloride	400 000
Trichloroethane	480 000
Methyl chloride	350 000
Chloroform	245 000
Chlorobutadiene	500 000
Ethylene dibromide	150 000 (USA only)
Epichlorohydrin	150 000 (USA only)
Vinylidene chloride	30 000

Apart from the direct entry of above-mentioned pollutants into surface water sources via insufficiently treated wastewater, water contamination can also occur through storage of solid and liquid wastes in waste dumps, or via influx of organic compounds (especially highly volatile halogenated hydrocarbons) from air due to rain wash-out [11-13].

A role not to be underestimated is played by migration from raw materials. In this connection, Bull has stressed the wash-out of vinylchloride from PVC-supply pipelines [14]. Monarca and Meier drew attention to the migration of components from bitumen-containing paints. Some of them, mainly polynuclear hydrocarbons, are known to be carcinogens and may present a risk which should not be underestimated by the consumer.

But particular importance is to be attached to those substances which are formed during drinking-water treatment, especially in the process of chlorination. In the following chapters some of these substances will be dealt with in detail.

3. Organic compounds being formed in the course of chlorination of drinking water (by-products)

The application of chlorine for disinfection of drinking water goes as far back as the 19th century after sewage already in the year 1800 had been treated with chlorinated lime in England and France [15].

The large-scale technical application of drinking-water chlorination was first performed in the United States of America at the beginning of this century [16]. It replaced the slow sand filtration having so far been used. Already in 1914, a large proportion of US cities was consuming chlorinated water [17].

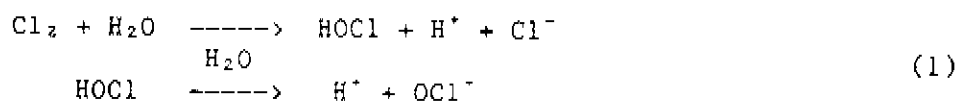
Despite all reservations, the introduction of chlorination of drinking water was not to be stopped. During the past 50 years, it has developed into the most widely used procedure for treatment of surface water, and it is performed in many countries as a "break-point chlorination" with subsequent sedimentation and filtration [18]. In addition to disinfection, which is the primary target, the use of reliable flocculation equipment will achieve a comprehensive removal of disturbing organic and inorganic constituents in nearly all waters [19,20].

Green and Stumpf investigated the biological activity of chlorine and established that in a concentration range between 0.2 and 2.0 ppm, chlorine will efficiently disinfect water [21]. They presented evidence that the disinfection effect of chlorine is based upon the fact that bacterial enzymes necessary for oxidation of glucose are blocked. The small chlorine molecules can penetrate the bacterial membrane of the cell and react with the glucose-oxidizing enzymes. A contact of half a minute is sufficient to reduce the bacterial oxidation of glucose by 95%, whereas a reaction time of 5 minutes is sufficient to kill bacteria. Chlorine is less effective for spores and bacteria which do not live in glucose oxidation.

Furthermore, chlorine proved to be an effective disinfectant for intestinal protozoa, schistosomes and a number of viruses, such as poliomyelitis and hepatitis viruses. Only a few germs, such as for instance the protozoon giardia lamblia, are resistant to chlorine [22,23].

Under natural conditions, chlorine is a gas which can be liquefied at room temperature. It can, therefore, be easily stored and transported. It is a very efficient oxidizing, bleaching and disinfecting agent.

In water, chlorine reacts as follows:



Hypochloric acid and hypochlorite ions represent the "free chlorine". This free chlorine reacts with a multitude of inorganic and organic compounds. This may be oxidation or incorporation of chlorine into the organic molecule, resulting in the formation of new chlorinated organic compounds. According to what is known today, approximately 90% of the added chlorine exercise an oxidating effect. Dependent on contact with organic micropollutants, the remaining 10% form halogenated organic reaction products.

A long time before identification and detection of such reaction products had become possible, reactions with organic micropollutants had already been presumed.

After Rook in the Netherlands and a little later Bellar et al. had established that chloroform and other trihalomethanes are formed during chlorination of surface water [3,4], a systematic search for by-products in drinking water after chlorination was started.

This was done not the least as a consequence of the so-called New Orleans Study carried out in 1974 [24] which presented evidence of highly volatile carcinogenic organohalogenes found in drinking-water samples and which gave rise to the first suspicions with regard to the correlation between stomach and/or bladder cancer and these micropollutants.

Since then, a large number of organic substances have been identified as by-products of chlorination of drinking water. The most important classes are [25-40] :

- trihalomethanes
- chlorinated phenols
- halogenated methanes, ethanes and ethenes
- haloacetonitriles
- halogenated polynuclear aromatic hydrocarbons
- chlorinated aldehydes and ketones.

3.1 Trihalomethanes (THM)

The occurrence of trihalomethanes in raw water and drinking water was confirmed in investigations carried out during the years 1974-1976 by Rook, Bellar et al., Bellar and Lichtenberg, Saunders et al., Dunlap et al., Koepfler, Suffet et al., Nicholson et al., Smillite et al. [3,4,41], and later by a host of other authors. Whereas THM occurred only occasionally and in small quantities in raw water, significantly increased concentrations were found after treatment (see Table 5).

Table 5. Trihalomethanes occurring in drinking water of American cities [42]

Substance	Average concentration (µg/litre)		Maximum concentration (µg/litre)	
	raw water	treated water	raw water	treated water
CHCl ₃	1	20	94	366
CHCl ₂ Br	1	6	11	51
CHBr ₂	1	1	1.4	14
CHBr ₃	1	1	1	7

This is an unambiguous confirmation of the hypothesis that these compounds are predominantly formed during chlorination of drinking water.

In general, it can be stated that THM have been found in nearly all analysed samples of chlorinated drinking water, with chloroform being the major constituent (see Table 6).

Table 6. Trihalomethanes occurring in drinking water [10]

Substance	Average concentration		
	USA	Canada	Federal Republic of Germany
Chloroform	21	22.7	6.4
Bromodichloromethane	6	2.9	3.4
Chlorodibromomethane	1.2	0.4	
Bromoform	5	0.1	

It was assumed that primarily humic substances can be considered as precursors for such compounds, since water predominantly containing humic acids showed high contents of THM after chlorination [3,27,43-45a,b].

The results of examinations using model waters were the basis for Rook's discussion on the possible role played by fulvic acids during the formation of THM [3]. The precise mechanism of reaction has not yet been fully established.

The amount of THM formed is directly dependent on the quantity of chlorine used, and is correlated with the content of organic carbon in a given raw water. It is worth mentioning that THM may even be formed within the water-supply system, with the residual chlorine in drinking water playing a decisive role [46].

3.2 Chlorinated phenols

In connection with chlorination of drinking water the appearance of chlorinated phenols very early become spectacular. This is a consequence of their deteriorating effect on odour and taste [47].

Already within a few minutes after chlorination of phenol-containing raw water, chlorinated phenols can be detected. The amount formed is dependent on the amount of chlorine used. During the chlorination, both oxidation of phenols and substitution of the nucleus occur. According to Morris halogenation goes on step by step, beginning at the 2nd, 4th and 6th positions [48]. The major part of the chlorophenols formed according to this mechanism is made up of 2,4-dichlorophenol (45%), trichlorophenol (40-50%) and monochlorophenol (4-10%) [47].

The amount of phenol required for the reaction may come from numerous different sources. In 1979, more than three million tons of phenol were synthesized on a worldwide scale [49]. Besides the anthropogenically

conditioned entry of phenols into water, their natural occurrence in the environment has to be considered as a source of input. Phenols come either directly from leaching of dead animal and plant matter, or are formed in the course of their microbial degradation, transformation and synthesis [50]. Besides cellulose, the most widely spread natural substance, lignin, being a polymerized phenol derivative, plays an important role. Table 7 presents the results of a survey on the concentrations of chlorinated phenols detected in drinking water.

Table 7. Chlorinated phenols occurring in drinking water

Substance	Concentration µg/litre
2,4-Dichlorophenol	0.003 - 0.006 [49]
2,6-Dichlorophenol	0.02 [49]
2,3,5-Trichlorophenol	0.001 [51,5]
2,4,6-Trichlorophenol	0.001 [51,5]
2,4,5-Trichlorophenol	0.003 [52]
2,3,4,5-Tetrachlorophenol	0.003 [49]
Pentachlorophenol	0.01 - 0.02 [49]

3.3 Halogenated methanes, ethanes and ethenes

Due to vast quantities produced (see Table 4), and the large field of application in different branches of industry, this group is frequently being referred to as "industrial organohalogenes".

However, it is very probable that a large proportion of these "industrial organohalogenes" are formed during chlorination of drinking water. Payne and Rahimtula support this opinion [10]. According to these authors, an indication therefore is the formation of such substances during chlorination of industrial sewage (see Table 8).

Table 8. Mutagenic halogenated methanes, ethanes and ethenes occurring in chlorinated sewage of paper mills [10]

Dichloromethane	1,1,2,2-Tetrachloroethane
1,2-Dichloroethane	1,1,3,3-Tetrachloromethane
1,1,1-Trichloroethane	1,2-Dibromoethane

Substances of this group are produced in large amounts, and they are formed on a large scale in the course of drinking-water chlorination. They are, therefore, frequently detected in drinking water, sometimes in considerable concentrations (see Table 9).

Table 9. Halogenated methanes, ethanes and ethenes occurring in drinking water

Substance	Concentration µg/litre	Reference
Dichloromethane	0.08 - 9.0	[53]
Tetrachloromethane	3.0	[54]
Chloroethane	0.15	[54]
1,2-Dichloroethane	8.0	[54]
1,1,2-Trichloroethane	0.1 - 8.5	[55]
1,1,1,2-Tetrachloroethane	0.11	[5]

Table 9. (continued)

Substance	Concentration $\mu\text{g/litre}$	Reference
Hexachloroethane	4.3	[54]
1,1-Dichloroethene	0.1	[42]
Chloroethene	10.0	[54]
Trichloroethene	113.0	[54]
Tetrachloroethene	0.4	[54]

3.4 Haloacetonitriles (HAN)

In 1976, Trehy and Bieber discovered the formation of dihalogenated chlorine and bromine derivatives of acetonitrile during drinking-water chlorination [56]. It was found that the amino-acids (especially tryptophan, tyrosine, kynurenine and aspartic acid), polypeptides containing aminoacyl-groups, and humic and fulvic substances with amino-acid particles in their circular structures are the precursors of HAN.

Oxidation with subsequent halogenation of amino-acids leads to the formation of HAN. During drinking-water chlorination mainly dichloroacetonitrile, dibromoacetonitrile and bromochloroacetonitrile are formed.

Trehy and Bieber found maximum dihaloacetonitrile concentrations of 42 $\mu\text{g/litre}$ in drinking water [56]. Table 10 presents the results achieved by Keith et al. who detected HAN in drinking water prepared on the basis of surface and groundwater [57].

Table 10. Concentration ($\mu\text{g/litre}$) of haloacetonitriles in chlorinated drinking water [57]

	Drinking water (1) (obtained from surface water)	Drinking water (2) (obtained from groundwater)	Drinking water (obtained from groundwater)
Dichloroacetonitrile	3	1	1.5
Trichloroacetonitrile	1	1	1
Dibromoacetonitrile	12.5	7	2

3.5 Chlorinated polynucleic aromatic hydrocarbons (PAH), chlorinated aldehydes and ketone derivatives

According to Schwarz et al. the occurrence of PAH in raw water is responsible for increased mutagenic activity occurring subsequent to chlorination of drinking water [46]. Oyler et al. examined the products of the aqueous chlorination reaction of 1-methylnaphthalene, fluorines, dibenzofuran, anthracene, phenanthrene, 1-methylphenanthrene, fluoroanthene, and pyrene [58,59]. They detected the formation of oxidized by-products at pH >6 reaction conditions (epoxides, phenols, quinones), and of both oxidized and chlorinated products which could not be identified in more detail under conditions of pH <6.

A number of chlorinated aldehydes and ketones were also identified as products of drinking-water chlorination. Due to their toxic properties 1-chloropropanol and 1,3-dichloroacetone are of special interest [14],

4. Health aspects of by-products of drinking-water chlorination

A quantitative evaluation of the examination of drinking-water chlorination by-products illustrated that, with only a few exceptions, concentrations of less than 1 µg/litre were to be found [60-62]. Koch and Tunger, and Stottmeister confirmed these findings for the German Democratic Republic [63,64].

It can be concluded that these substances will not produce any acute toxic effects in relation with drinking water. In contrast to occupational exposure to such substances or to their intake with foodstuffs, the important health-related impact of their ingestion can be described as follows:

- intake takes place over the entire lifespan, beginning at the prenatal phase and ending at death;
- this goes for persons of all age groups with different genetic predispositions and different states of health and disease;
- trace amounts in the microgram range are ingested;
- a complex mixture of these substances is ingested at one and the same time.

Under such conditions, effects on health, especially irreversible mutagenic and/or carcinogenic long-term effects, have to be expected.

Hygienists have expressed great concern about the mutagenic substances present in the human environment.

Some of the reasons for this are:

- the obviously existing primary connection between these substances and the occurrence of hereditary diseases in man. Kool et al estimated that at least 10% of all pathological conditions in man are caused by genetic factors [65];
- there is evidence that approximately 15% of all premature births and stillbirths are linked to alterations in the genetic material, with the rate of spontaneous miscarriages occurring before the 16th week being 50% (chromosomal anomalies) [66];

- one has to start from the assumption that the mechanism of carcinogenesis involves somatic mutations, and that for a considerable number of carcinogens (70-80%) mutagenic effects have been established.

After the detection of carcinogenic substances in the New Orleans drinking water in 1974, Page et al. investigated the relationship between cancer mortality rates and drinking water which had been obtained from the Mississippi River [67]. A definite correlation seems most probable. Thirteen additional studies were carried out thereafter, inter alia, by Dowty et al. [68a,b], Ibrahim and Christmas [69], Kuzma et al. [70], and Cantor et al. [71].

The results of these studies were summarized by the Epidemiology Subcommittee of the Safe Drinking Water Committee of the National Academy of Sciences, USA, as follows [72]:

The examinations lead to the conclusion that increased concentrations of THM in drinking water are correlated to an increasing frequency of bladder cancer. The examinations do not reveal any cause-effect relationship and the quantitative evaluation of an increasing or decreasing cancer risk is extremely imprecise.

Within two years, 20 further studies of this kind were carried out all over the world [60,73-77,62].

Many studies confirmed the definite correlation between the quality of drinking water and various cancer mortality and/or morbidity rates. Williamson draws the conclusion that these studies obviously support the hypothesis that an increased risk of cancer of the bladder, intestines and rectum does exist for those persons who consume drinking water containing organohalogens, especially THM [78,79].

5. Mutagenic effects of by-products

Within the past few years numerous papers have been published presenting evidence of mutagenic effects of chlorinated drinking water, as detected in short-term tests, especially the Salmonella-microsome-assay [80-96].

Different concentration procedures have been applied in order to give proof of the mutagenic effect in the test system used (e.g. Amberlit-resins, liquid-liquid extraction, reverse osmosis). It was unambiguously demonstrated that drinking water, especially when the raw water was heavily polluted by organic substances, had a significantly higher mutagenic activity after chlorination than prior.

In this way, direct mutagens, and promutagens as well, were detected. Besides base-pair substitutions, frameshift-mutations can also be induced by them.

By means of analytical identification methods (GCMS), single substances were identified in these complex mixtures and examined for their mutagenic activity.

Helms et al. published a list of substances which are formed in connection with chlorination of drinking water and have been identified as mutagens by means of the Ames test [97] (see Table 11).

 Table 11. Mutagenic by-products of drinking-water chlorination (Ames test) [97]

1-bromo-2-chloroethane	Dibromoethane
Bromochloromethane	Dichloroacetonitrile
Bromodichloromethane	Bromochloroacetonitrile
Bromoform	1,2-dichloroethane
Bromoethane	Methylen chloride
Dibromochloromethane	Trichloroethylene
1,1,2,2-tetrachloroethane	1,1,2,2-tetrachloroethylene
1,1,1-trichloroethane	1,2-dibromoethane

Investigations confirmed these results in an Ames test and further by-products were identified as mutagens [98a,b,c] (Table 12).

 Table 12. Mutagenic by-products of drinking-water chlorination (Ames test) [98a,b,c]

Bromochloromethane	1,1,2,2-tetrabromoethane
Dibromomethane	1,1-dichloroethene
Dichloromethane	1,2-trans-dichloroethene
Bromodichloromethane	1,2-dibromoethene
Bromotrichloromethane	1,1,2-trichloroethene
1,2-dichloroethane	3-chlorophenol
1,2-dibromoethane	4-chlorophenol
(mono)-bromoethane	2,3,6-trichlorophenol
1,1,1-trichloroethane	2,4,5-trichlorophenol
1,1,2-trichloroethane	2,4,6-trichlorophenol
1,1,1,2-tetrachloroethane	4-chloro-2-methylphenol
1,1,2,2-tetrachloroethane	4-chloro-3-methylphenol

6. Alternative procedures for drinking-water disinfection and health implications

The formation of by-products in the course of chlorination of drinking water, and the detection of mutagenic/carcinogenic effects, gave rise to manifold discussions among both the experts and the public [99].

The clear advantage of a reliable disinfection of pathogenic microorganisms must be weighed very carefully against possible disadvantages, in order to be able to consolidate and to make the necessary decisions.

Therefore, the search for "alternative" procedures for drinking-water disinfection has become a priority nowadays. New procedures for disinfection are not of as much importance as the evaluation of already existing procedures in wide-scale use and for which a new evaluation is necessary in view of the formation of toxic by-products.

6.1 Chlorine dioxide

With regard to disinfection, chlorine dioxide is as effective as chlorine [100] or even superior to it [101]. Furthermore, its application does not cause any deterioration of taste. It is a relatively stable compound in water, and its disinfecting efficacy is largely pH-independent. The formation of THMs can virtually be neglected [102]. However, the formation of polar compounds, such as aldehydes, ketones, acids [103], should be taken into account, as well as various isomeric chlorophenols, such as 2,4,6-trichlorophenol which shows carcinogenic effects in animal tests [104]. In contrast to other disinfectants, chlorine dioxide forms toxic inorganic compounds in use, a fact which should not be neglected. It has been established that 50% of the used chlorine dioxide is transformed into chlorite (ClO_2^-) and 25% to chlorate (ClO_3^-). These substances will provoke methemoglobinaemia in babies if concentrations in drinking water exceed the value of 0.1 mg/litre [105,106]. According to Bull, this develops as follows: the cellular membrane is damaged, with glutathione being exhausted at the same time as hydrogen peroxide is increasing [107]. Contrary to the effects of nitrite, this leads to haemolytic anaemia. According to Stachel, an increased rate of cell division and an impaired spermatogenesis will probably occur at concentrations of 10 mg chlorine dioxide per litre [104].

Studies of mutagenic activities revealed that at concentrations of less than 1 mg chlorine dioxide per litre, no increase in the mutagenic activities in drinking water occurs, whereas there is a significant increase in mutagenic activities at high doses [108-112].

It has to be added that costs of treatment of drinking water with chlorine dioxide are three to four times as high as chlorination [113].

6.2 Chloramines

Compared to chlorine dioxide, chloramines are less effective disinfectants [114,100] and, furthermore, have an algicidous effect. Their efficacy is heavily dependent on the pH-value, a higher efficacy having been observed at lower pH-values.

A major disadvantage of chloramines in drinking water is their deteriorating effect on taste and odour. According to Krasner and Barret, the threshold levels are 0.15 mg/litre for taste and 0.13 mg/litre for odour [115].

So far, direct health-related effects of chloramines have hardly been studied. Komorita and Snoddyink have pointed out that haemolytic anaemia under the influence of chloramine has been observed in dialysis patients [106].

However, health implications arising from the application of chloramines seem to be connected with the protolytic degradation of chloramines, the consequence of which is freely available chlorine which, although not in the same degree as for chlorination, is able to form toxic by-products [114].

6.3 Ozone

Ozone is a strong oxidant and disinfectant. Its relative oxidizing potential for chlorine is 1.52 [116]. Special advantages of ozone are:

- improvement of odour and taste
- transformation of almost indegradable substances into easily degradable ones (due to the high redox-potential)
- microfloculation effect.

Disadvantages are regrowth within the water supply system and formation of a number of toxic compounds. Ozone is able to degrade such health-impairing substances as PAH, phenols and chlorophenols. However, not all organic compounds will be reduced or even mineralized. Ozonization of benzol derivatives and higher aromatic hydrocarbons, therefore, results in a broad variety of organic compounds, such as alcohols, aldehydes, ketones, carbon acids, peroxyacids, ozonides, and epoxides [117], quite a number of which may be mutagenic and/or carcinogenic [118-120].

Table 13 presents a survey on the hitherto unknown formation of organic compounds which was detected in the course of ozone treatment of surface water.

Table 13. Effects of ozone treatment of bank filtrates in µg/litre [121]

Compounds	before ozone treatment	after
Bis-(2-chloroethyl)-ether	30	30
Bis-(2-chloroisopropyl)-ether	1000	1000
Chloroaniline	1000	300
Chlorotoluidine (ortho)	100	30
Chlorotoluidine (para)	10	10
Chloroform	180	500
1,2-dichlorobenzol	10	300
1,3-dichlorobenzol	30	100
1,2-dichloroethane	500	500
1,2-dichloropropane	-	30
Monochlorobenzol	10	30
Tetrachloromethane	100	800
Tetrachloroethene	50	-
Trichlorobenzol	300	100
Trichloroethene	130	100

Ozonization of pesticides which are present in water may result in the formation of toxic metabolites. Epoxides, for instance, are formed from DDE, heptachlorine, and aldrin [122]. Hoffmann and Eichelsdörfer detected the formation of oxones originating from parathion and malathion [123]. There was also evidence of formation of bromoform during ozone treatment of water containing bromide (for instance effluents of the potash industry) [124].

Studies on the mutagenic activity of drinking water after ozone treatment gave conflicting results. For instance, Dolara et al., Van der Gaag et al., Bourbigot et al., Dugnet et al., and Van Hoof et al. reported an increase in the mutagenic activity after ozone treatment [125-129]. Conversely, Zoeteman et al. detected the complete disappearance [110], and Dolara et al., and Kool et al. a drastic reduction of the mutagenic activity in drinking water after ozone treatment [130,125,88,112,112,82,99]. These results give rise to the assumption that variations in the mutagenic activity depend strongly on the

conditions under which the procedure is performed. Apparently, a reduction of the mutagenic activity seems to be linked to a high ozone level which is active over a long period of time.

7. Conclusions

A critical evaluation of alternative disinfection procedures has revealed that the ideal disinfectant does not yet exist. All known disinfection procedures practicable on a large scale will in the course of the disinfection process lead to formation of by-products which are all hazardous to health, and quite a number of which are mutagenic and/or carcinogenic.

The cause of the formation of such toxic by-products is one and the same for all disinfection procedures, i.e. the presence of organic precursors in the raw water. Consequently, prophylactic measures have to be implemented at this point in order to prevent or at least minimize the formation of by-products. Removal of by-products after their formation is neither a logic approach, nor an economic one, especially since reliable procedures for their removal are not yet available.

In principle, two main procedures may be chosen to keep organic precursors at a minimum:

- a. removal of organic substances from raw water by means of special treatment procedures prior to disinfection;
- b. use of raw water which already contains organic precursors at such a low level that the formation of toxic by-products in any significant quantities can almost be excluded.

Some countries (e.g. the Netherlands) prefer the former possibility, not the least because of the special geographical conditions. Infiltration into layers of soil, open and aerated reservoirs, slow sand filtration, especially in the dunes, are measures taken in order to reduce the content of organic matter drastically.

From the point of view of prophylaxis, the latter is preferable. It envisages prevention at the very source of damage and therefore is the more effective measure. The protection of water resources from contamination by organic matter can be carried out either locally in sewage treatment plants for domestic and industrial sewage, or regionally by designation of protected areas for drinking water. This seems to be not only the more effective, but in the long run also the more economic way of keeping the contamination of drinking water by toxic disinfection by-products at a minimum.

At the same time, it is necessary to determine limit values for toxic by-products from drinking water disinfection. At present, such values are the most effective instrument for reducing the health-related risks from exposure of man to environmental pollutants. A prerequisite for introducing norms for pollutants is the establishment of threshold values for toxic effects which depend upon quantity of substance and exposure time. But for mutagenic and carcinogenic substances, the existence of such a threshold level is vigorously disputed these days. There are very good reasons for supporting the establishment of threshold levels, but there are equally as good reasons for objecting to it. The uncertainty in connection with the lack of threshold levels for mutagenic/carcinogenic substances has had as a result that in extreme cases either no limit values have been established, or those established fail to take specific toxic effects into consideration.

In the interest of the protection of human health, the establishment of threshold levels for mutagenic/carcinogenic substances can no longer be postponed. The technically possible and economically practicable reduction of potential hazards caused by mutagenic/carcinogenic substances must be achieved as soon as possible, and in spite of gaps in our knowledge, the World Health Organization has worked out a solution to the problem. WHO has been concerned with the problem since 1974, and in 1984 "Guidelines for Drinking Water Quality" for the first time presented recommendations for the determination of guideline values for mutagenic/carcinogenic substances in drinking water which subsequently have been adopted by a number of countries (see Table 14).

Table 14. Guideline values and tentative guideline values for health-related organic constituents [2]

Compound	Guideline value ($\mu\text{g}/\text{litre}$)
1,1-dichloroethylene	0.3
1,2-dichloroethane	10.0
2,4,6-Trichlorophenol	10.0
Hexachlorobenzene	0.01
Benzo-a-pyrene	0.01
Benzene	10.0
Chloroform	30.0
Trichloroethylene	30.0 (tentative)
Tetrachloroethylene	10.0 (tentative)
Carbon tetrachloride	3.0

When these guideline values were established, WHO started out from the position that carcinogenic and mutagenic substances are subject to the same physicochemical and biological interactions assumed to be essential for the threshold levels for other chemicals [131]. Results obtained in animal tests with high dose-ranges were extrapolated to low dose-ranges which correspond to ranges relevant to human exposure. This is the basis for the formulation of these guideline values. Nowadays mathematical-statistical models are used which start from the assumption that in a low-dose range, the dose-response curve follows a linear function. In the present case, the "multistage model" has been applied, which takes into consideration both the assumption of a multifactorial mechanism in the process of the development of tumours and the spontaneous probability of the occurrence of tumours. The acceptable lifetime risk of 1 : 100 000 has been selected arbitrarily. Similar approaches by Stara et al. already in 1980 led to the proposition of limits for mutagenic and carcinogenic substances in water [132].

Consequently, pursuing its strategy during its Consultation on potentially microorganic substances in drinking water in Medmenham, WHO selected further substances for which tentative guideline values have to be established using the same method [133]. It will be useful if these values be incorporated without delay in the Guidelines for Drinking-Water Quality.

Only recently, various other aspects have come to light which so far have been underestimated in the evaluation of human health risks caused by drinking water by-products. For instance, besides direct intake of these substances in water, one also has to take into consideration that quite a considerable amount of them is being inhaled from the use of drinking water in households, for daily hygiene, in swimming pools, and at special work places.

This applies especially to highly volatile substances. Andelmann, and Wallace et al. have carried out studies which confirm these facts [134,135]. Table 15 illustrates the findings from a survey on the daily consumption of drinking water in households, listed according to the purpose of use. It has to be taken into account that, since 1973, this consumption has increased by at least 50%.

Table 15. Typical daily domestic use of water per capita in the United States of America [136]

Use	Quantity per capita per day (litres)
Drinking and cooking	4 - 8
Dishwashing	4 - 15
Garbage disposal unit	0 - 15
Laundering, cleaning	11 - 34
Bathing	38 - 95
Toilet	91
Total	148 - 257

According to these data for a family of four persons, an indoor load of volatile by-products from more than 1000 litres of drinking water can be assumed. Measurements of the out- and indoor concentrations illustrate that for some highly volatile organohalogens the exposure levels are quite considerable (see Table 16).

Table 16 Comparison of outdoor and indoor air concentrations of chlorinated methanes [137]

Substance	Concentration in the air (ppt)	
	outdoors	indoors
Dichloromethane	390 - 6 760	170 - 14 000
Chloroform	81 - 900	14 - 730
Carbon tetrachloride	130 - 400	140 - 460

When determining exposure, one has to start from the fact that the volume of air of a man's daily breathing amounts to 23 m³, that of a woman to 21 m³, that of a 10-year old child to 15 m³, and that of a 1-year old infant to 3.8 m³ [138]. Wallace et al. established the daily intake for 15 volatile organohalogenes via air and drinking water [135]. They found that apart from chloroform and bromodichloromethane, the daily intake of all other compounds via breathing was higher than via drinking water (>80% of the total amount ingested). They established the average total daily intake of volatile organohalogenes which ranges between 0.3 and 12.6 mg, with the biggest proportion occurring for 1,1,1-trichloroethane.

8. Summary and Recommendations

- It is incontestable that the drinking water chlorination represents one of the biggest successes of sanitation achieved in this century. With the appropriate application of this method, waterborne infectious diseases, such as typhoid fever, infectious hepatitis, dysentery and cholera were decisively restrained.
- Since Rook's discovery of the formation of a number of highly toxic substances (e.g. THM) during drinking-water chlorination [3], obviously the reverse side of this method became apparent.
- Comprehensive studies carried out all over the world illustrate that the THM discovered by Rook are obviously only the top of the iceberg. Nowadays it is known that a multitude of by-products (e.g. halogenated methanes, ethanes, ethenes, chlorinated phenols, chlorinated PAH, chlorinated aldehydes, ketone derivatives, and haloacetonitriles) are formed in the course of drinking-water chlorination by transformation of their organic precursors.
- The quantitative studies of these substances have revealed that acute toxic effects cannot be expected. Today, it is known that a large proportion of these substances have mutagenic and/or carcinogenic properties, thus being potential hazards to human genes and the cause of malignant tumours.

- A comparison with "alternative" drinking water disinfection procedures (chloride dioxide, chloramine, ozone) reveals that in all other procedures, by-products are formed which constitute a considerable health hazard and are able to provoke mutagenic and/or carcinogenic effects. It does not seem that a genuine alternative for the chlorination of drinking water exists.
- Since for reasons of prevention and control of epidemics the disinfection of drinking water cannot be dispensed with, all prophylactic measures must concentrate on the reduction of the content of organic precursors.
- The reduction of the amount of organic precursors can be achieved using appropriate technologies for the treatment of raw water (e.g. infiltration, open, aerated reservoirs, slow sand filtration) and by optimal protection of the water resources (sewage treatment plants, protective zones for drinking water reservoirs). In the long run, the protection of drinking water resources seems to be the most effective and economic way to keep the pollution of drinking water by disinfection by-products at a minimum level.
- It is recommended to control such protective measures regularly with appropriate test systems, and also control the raw water quality. This applies also for drinking-water quality in large drinking-water supply systems. The Ames-test in connection with effective, specific concentration methods seems to be appropriate and sufficient.
- Apart from this, regular control of the total mutagenic activity in water and analytical surveillance of selected single substances are also necessary.

The attempts to establish limit values for mutagenic/carcinogenic substances, made by WHO in its Guidelines for Drinking-Water Quality, must be pursued systematically to limit further substances from the group of by-products effectively.

The corresponding activities should be included in the Post-Decade Strategy of the IDWSSD of WHO.

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