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POTENTIALLY TOXIC MICROORGANIC SUBSTANCES IN DRINKING-WATER

Report on a Consultation

Medmenham, United Kingdom
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EUR/HFA target 20

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.

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1. INTRODUCTION

The Consultation was convened by the Regional Office for Europe of the World Health Organization (WHO/EURO) and jointly organized by WHO/EURO and the Water Research Centre (WRc), a WHO collaborating centre. The meeting was held at the Medmenham Laboratory of WRc, in the United Kingdom.

The participants were welcomed by Mr M.J. Rouse, Chief Executive of WRc, and the Consultation was opened by Professor R.F. Packham on behalf of the host institution. Mr J.O. Espinoza Cajina, Regional Officer for the International Water Decade, greeted the participants on behalf of the Regional Director of WHO/EURO.

The Consultation was attended by fifteen participants from nine countries (Canada, Federal Republic of Germany, France, Hungary, Japan, The Netherlands, Poland, United Kingdom and United States of America) representing national institutions concerned with the quality of drinking water and environmental health. The disciplines of the participants included chemistry, toxicology, public health, water engineering and statistics. A number of them had previously been involved in the development of the Guidelines for Drinking Water Quality (WHO 1984).

2. SCOPE AND PURPOSE

The recommended guideline values for micro-organic compounds in drinking water contained in the WHO Guidelines for Drinking-Water Quality 1984 were compiled in 1980. Because of the limitation in available toxicological data for a number of important water contaminants, some compounds were allocated 'tentative' guideline values only. It was recognized that with the passage of time advances in toxicological data, plus the possibility that new micro-organic compounds of potential significance to public health may be identified as drinking water contaminants, would necessitate a reassessment of the problem. In the last few years there has been increasing concern within the European Region about contamination of drinking water by small concentrations of toxic substances. The Regional Office was therefore requested to carry out an appraisal of the situation.

The Consultation agreed to address the following tasks:

(1) To review the methods used in setting and presenting guidelines for health-related organic compounds in drinking water.

(2) To indicate whether there exists significant additional toxicological information that ought to be taken into account in reviewing the guide levels for the compounds for which tentative or firm guidelines were previously set.

(3) To agree the criteria for selecting (new) substances as worthy of consideration for guidelines to be set.

(4) In the light of (1), (2) and (3) to list those substances which merit review with a view to development of WHO guideline values.

(5) To make recommendations on how the review should be undertaken.

3. BACKGROUND INFORMATION

The World Health Organization (WHO) published its Guidelines for Drinking Water Quality (referred to henceforth as 'the Guidelines') in 1984, based on the deliberations of a number of task groups convened between 1978 and 1982. For organic contaminants the selection of compounds was discussed at a consultation meeting at Leidschendam in the Netherlands in March 1980 and the guideline values were determined by a task group that met in Ottawa in November of the same year.

In the Preface to Volume 2 of the Guidelines it was recognised that as new information became available the recommended guideline values would have to be reviewed and revised. The need for this is particularly apparent for the organic compounds because of the technical difficulties of setting guidelines for them from toxicological information that is inevitably limited. In view of this, any additional knowledge, of either the mode of action or the strength of an effect, could have an important bearing upon whether, and at what level, a guideline should be set.

Since 1980 a number of other important documents concerned with environmental standards have appeared (eg, air quality guidelines (WHO/EURO), environmental health criteria (IPCS), IARC monographs), many dealing with chemicals that occur in drinking water. It would be appropriate to take these into account in considering new or revised guidelines for drinking water. Furthermore, several countries have produced their own national guidelines or standards for drinking water based on original toxicological reviews. These assessments are an additional and valuable source of data relevant to the development of guidelines for micro-organic pollutants in drinking water.

In 1980 there were three compounds for which tentative guideline values were recommended; the status of these compounds needs, if possible, to be resolved.

For all of the above-mentioned reasons the guidelines for organic contaminants should be revised. This attention to the organic constituents of drinking water should not, however, be allowed to exaggerate their importance relative to other aspects of water quality. The probability and potential consequences of microbiological contamination are such that its control must always be of paramount importance and this is relevant when considering the chronic health implications of any organic by-products of disinfection processes.

The Consultation believes that the WHO Guidelines have been well accepted throughout the world although subject to different interpretation depending upon the degree of development. Some countries have tended to accept the guidelines literally and without consideration of local conditions. The 'tentative' nature of some of the guideline values also raised conceptual difficulties.

4. CONCEPT AND PURPOSE OF GUIDELINES

4.1 The evolution of guidelines

The idea of setting numerical limits for chemical constituents of drinking water, to safeguard public health, has a lengthy history. Nevertheless the formulation of recommendations for the quality of drinking water, is an ongoing process as new data and related information becomes available. The WHO Guidelines will therefore almost certainly undergo continuing development. This means that in any exercise designed to capture the best advice available at a given instant, it is necessary to strike a balance between continuity with previous recommendations and the recognition that it may no longer be best to do things in exactly the same way as hitherto.

The development of guidelines takes place not only as better data and improved methods of assessment become available, but also as the ways that people use the concept of 'guideline' evolve with time. An important step in this evolution was evident in the Guidelines (WHO 1984), which avoided the rather rigid and authoritarian stance of the previous WHO standards, in favour of a more flexible view of the way that the new Guidelines would be implemented. The WHO intended that national legislation would reflect a more thoughtful approach to applying the guide levels rather than slavish adherence to them.

The nature of 'guideline values' was explained in Section 1.3 of Volume 1 of the Guidelines in a series of eight statements. It is particularly relevant to recall two of these:

> "(a) A guideline value represents the level (a concentration or a number) of a constituent that ensures an aesthetically pleasing water and does not result in any significant risk to the health of the consumer."
>
> "(g) In developing national drinking water standards based on these guidelines, it will be necessary to take account of a variety of local, geographical, socioeconomic, dietary and industrial conditions. This may lead to national standards that differ appreciably from the guideline values."

The different conditions that could influence the adoption of different standards in different countries include not only factors that might influence the intake, uptake or effects of the relevant chemical compound but also the country's own risk/benefit criteria. Hence it was recognised in the Guidelines (Section 1.4) that national standard-setting involves considerations not only within the sphere of environmental and medical sciences but also extending to questions of economic and political choice.

The selection of a national standard at a level that is somewhat higher than the guideline value does not necessarily imply that the water would not be safe enough. The safety (or uncertainty) factors incorporated in the guideline value may be more than enough to accommodate some compromise for the sake of practicality, without having any effect on public health, but this depends on judgement of the particular case, based on a full understanding of the way that the guideline value was derived.

4.2 Flexibility and the need for explanation

The concept of a 'guideline value' is deliberately intended to imply flexibility but, in order to exercise that flexibility, it is necessary that users of the Guidelines be given information (a) on how the guideline was calculated and (b) on how the underlying assumptions may be varied if it is appropriate to do so (for example by adopting a different level of 'acceptable risk'). Volume 2 of the 1984 Guidelines provided some of this information but, as will be indicated later, there are aspects of the criteria which would be more useful if they were made still more explicit.

Of the ways in which guidelines may be presented to enable flexibility of use, one possibility - and a way of satisfying both the need for flexibility and the clamour for single numbers - would be to present the derivation of a guideline value conditional on certain assumptions, but with enough supplementary information to enable the user to vary the assumptions if he wishes. These assumptions, especially where falling within the scope of risk management, rather than science, could be declared as 'default assumptions'. The onus would not then be on WHO to justify these assumptions - a task that would be impossible anyway in a world context - but on national standard-setting organisations which would take responsibility for accepting these assumptions or, in particular, for departing from the 'default' values if they wished to set a numerical standard different from the guideline value. The Consultation recommends that these 'default' assumptions be made more visible, possibly through summarization in tabular form.

4.3 Rounding

The 1984 guide values for organic contaminants were all rounded to points on a logarithmic scale on which each step corresponded to an increase of half an order of magnitude. The rules by which the direction of rounding was decided were not, however, consistent nor completely clear.

The Consultation agreed that, in principle, some rounding is desirable in the presentation of guide values. If this is done, the text of the criteria document should still contain the unrounded result, for reference, so that it may be used in any further calculations without loss of accuracy. The revised criteria document should contain a section or an appendix which sets out the rules by which any rounding has been performed, but the Consultation did not decide what those rules should be.

4.4 Issues addressed by the Consultation

Whichever way is chosen for presenting the guidelines and their supporting information it is important that the reasoning be both complete and explicit. In order to achieve this there are a number of issues to be addressed in the guideline documentation. The list of these topics corresponds closely with the issues considered by this consultation which were as follows:

- the nature and degree of the potential health hazard;

- the models and techniques that are used for estimating the risk at low doses of substances that are believed to be genotoxic carcinogens;

- the use of the notion of 'acceptable risk' in setting guidelines and the preferred terminology for this concept;

- the assumptions that are made about human exposure to organic compounds in drinking water and exposures from other routes;

- how numerical values should be presented, with particular attention to the question of rounding.

In addition the criteria for selecting compounds were discussed and a list of compounds was developed, based on these criteria, that the Consultation recommends to WHO for early reconsideration.

5. TOXICOLOGICAL CONSIDERATIONS

5.1 Introduction

The setting of health-related guideline values for organic contaminants in drinking water, involves the use of data derived from epidemiological investigations, experiments with laboratory animals and supporting data from in vitro studies. There are a number of difficulties in this process, including extrapolation from animal to man and from high doses used in laboratory experiments to low exposures via drinking water.

One of the major reasons for differences in sensitivity between species may be differences in metabolism and pharmacokinetics. Species may handle a compound by different metabolic routes or by the same route but at different rates. These differences may compromise the extrapolation from one species to another.

There is also a range of sensitivity or susceptibility to toxic effects, within an exposed population. This may be due to genetic variation or to differences in physiology, exposure or existing disease. This gives rise to special groups which may be at particular risk, for example babies or young children and individuals with kidney or liver insufficiency.

It has been traditional to calculate dose on the basis of body-weight for the purposes of inter-species extrapolation. Increasingly body-surface area is being used as a basis for calculating dose, for example in low-dose extrapolation models for carcinogens. In some cases this may reflect more accurately the differences between species than body-weight, but the decision as to which approach to use must be taken on the basis of individual chemicals.

In examining cancer as an end-point there are additional considerations, among which are type of tumour, site of tumour and exposure route. The relevance to human cancer of tumours which are commonly found in experimental populations of rodents is generally considered to be high. However there is a particular problem when interpreting the nature of proliferative changes in mouse liver and rat kidney. In addition there is incomplete agreement about the classification of tumours as malignant or benign.

The route of exposure may have a significant effect on toxicity or carcinogenicity. Caution must therefore be exercised if toxicity or carcinogenicity data derived from exposure by one route is to be applied to circumstances of exposure by another route.

A further consideration when examining toxicity data is the effect of the vehicle used to dose the compound under study. There is mounting evidence, for example for volatile halogenated hydrocarbons such as carbon tetrachloride and chloroform, that dosing in a vehicle such as corn oil can change the toxicity and carcinogenicity compared with dosing in an aqueous vehicle.

5.2 Toxicological basis of extrapolation - mechanistic considerations

The use of mathematical models for low-dose extrapolation involves some fundamental differences of approach from the traditional application of uncertainty factors (often referred to as 'safety factors') to no observed effect levels in animal studies. For most toxic effects arising from exposure to chemicals it is believed that there is a dose, or threshold, below which adverse effects will not occur. For other toxic effects, cancer in particular, it is hypothesized that there is some probability of harm at any level of exposure although this is assumed to be very small at low levels of exposure. In addition cancer is usually a disease which will continue to progress even after the chemical insult is withdrawn.

It has therefore become quite usual to establish standards or guidelines for carcinogens on the basis of estimated risk at very low doses. The techniques used in this process are discussed in more detail in Section 6. They are based on mathematical models of the biological processes underlying chemical carcinogenesis. Such models, when applied to carcinogenic compounds of moderate chronic toxicity, as measured by tissue damage, have frequently led to much lower acceptable concentrations in water than would result from using the uncertainty factor approach, and this may have a substantial impact on the operations of water supply authorities. The justification for using a particular approach should be carefully considered for each compound.

5.3 Target organ toxicity

For most organ-specific toxicity including reproductive and behavioural toxicity it is generally believed that there is a dose below which no adverse effects will occur, because of physiological reserve capacity and protective mechanisms within the organism at both tissue and cellular levels. It is considered that the application of an uncertainty factor will then provide an adequate margin for the derivation of the standard or guideline.

The application of uncertainty factors has been widely used in the derivation of acceptable daily intakes (ADI) for food additives pesticides and environmental contaminants. A factor of 100 (made up of 10 for extrapolation from laboratory animals to man and 10 for the potential range of sensitivity in the human population) has frequently been applied to the no observed adverse effect level (NOAEL) in animal studies although other uncertainty factors have been used where justifiable. This approach was used by the United States National Academy of Sciences in calculating suggested 'no-adverse-effect-levels' for contaminants in drinking water.

Uncertainty factors to be applied to the lowest no observed effect level for the response that is considered to be most biologically significant can be derived in a number of ways, for example Table 1.

Table 1. Derivation of 'Uncertainty' factors

Source of uncertainty	Factor
Interspecies variation	10
Intraspecies variation	10
Nature and severity of effect	1-10
Adequacy of study	1-10
Interactive effects	1-5

The selection and application of uncertainty factors is important in the derivation of standards or guideline values for chemicals, since the limit set can vary by one or two orders of magnitude on account of these factors. There is merit in using a method which allows a high degree of flexibility but it is highly desirable that the derivation of the uncertainty factor used in calculating a guideline value should be clearly presented as part of the rationale.

5.4 Carcinogenicity

The initiating event in the process of chemical carcinogenicity is often considered to be the induction of a mutation in the DNA of a somatic cell. In some cases the chemical acts directly on the DNA; in other cases it may require activation by the metabolic system. This process theoretically has no threshold. This is the basis and rationale for mathematical models for low-dose extrapolation. Although one can propose mechanistic reasons, such as DNA repair and immune surveillance as well as pharmacokinetics, for a threshold to exist in some cases, it is not possible to prove or disprove this by experiment.

There are, however, some types of carcinogens which are capable of producing cancer at high doses in animal studies but which cannot be shown to have genotoxic activity. In these cases, the mode of action is probably either cytotoxicity in the target organ, with the resulting tissue repair increasing the possibility of spontaneous mutation, the promotion of previously initiated cells, or the deregulation of metabolism. If the mechanism of action of non-genotoxic carcinogens depends on tissue damage, then a threshold dose will be apparent and the use of low-dose extrapolation models would be inappropriate.

The Consultation considered that the use of low-dose extrapolation models is an appropriate method of determining guide values for known or probable human carcinogens unless there is convincing evidence to suggest that a non-genotoxic mechanism would be a preferable assumption. Where the evidence for the carcinogenicity of a chemical is weak or equivocal it may be considered inappropriate to apply low-dose extrapolation. The WHO Drinking Water Guidelines should be developed by an analysis that includes a qualitative assessment of the evidence, followed by a quantitative determination. The qualitative assessment, using a procedure such as the

current IARC guidelines, would classify all substances into categories ranging from 'known human carcinogens', to 'non-carcinogens' with 'animal carcinogens', 'limited or equivocal evidence' and 'insufficient evidence' in between. Drinking Water Guidelines for those substances ranked in the 'probable' or 'known' categories should be quantified using the risk extrapolation methodology; those in the 'insufficient' or 'non carcinogen' categories should be quantified using standard ADI calculations (NOAEL modified by uncertainty factors); those in the 'limited or equivocal' category should be calculated using the ADI modified by an additional uncertainty factor.

6. LOW-DOSE EXTRAPOLATION

6.1 Risk-related guidelines for carcinogens

One way of determining a guideline value for a carcinogenic substance in drinking water involves estimating the relationship between the concentration of the substance and the consequent risk to human health. This estimation almost always has to be based on the results of animal tests carried out with very much larger doses than would ever be experienced in the consumption of drinking water by man. The dose-response relationship has therefore to be 'extrapolated' from high to low doses. The results of the assay have to be assumed to be transferable between species and the measurement of dose has to be translated into an equivalent concentration of the substance in drinking water consumed by man. From this relationship, between concentration and hypothetical risk, a concentration can be determined so as to ensure that the damage to health is kept below some declared 'acceptable' or 'negligible' or '*de minimis*' level of risk.

Risk-related methods have begun to be used by several agencies to estimate the impact of water-quality standards on human health. In particular the 1984 Guidelines included guideline concentrations for seven organic contaminants, which were derived from the results of animal carcinogenicity studies by risk extrapolation. The same procedure was used for setting tentative guide values for a further three compounds.

6.2 Approach taken in the 1984 Guidelines

For the low-dose extrapolation, the 1984 Guidelines adopted the linearized multi-stage model, and the guideline concentration was determined as that for which the one-sided upper 95% confidence limit on risk was 10^{-5} per lifetime.

The assumptions on which these calculations were based were not fully explained, and little was said to justify the choice of the multi-stage model, or the use of a confidence limit as the statistic on which the guideline value was based.

The level of 'acceptable risk' of 10^{-5} per lifetime was stated to be "arbitrarily selected" (Volume 1, p62) and earlier the text said,

"The cancer risk associated with other concentrations of these substances can be readily calculated" (Volume 1, p51).

Readers were not, however, told exactly how to do such a calculation, nor were the Guidelines completely explicit on whether readers were expected to exercise the option of modifying the guideline values in this way, although it is clear from the spirit of the documents and from explanation elsewhere that such an interpretation was intended.

6.3 Use of low-dose extrapolation in revising the guidelines

The Consultation discussed the methods and assumptions of low-dose extrapolation that should be used in preparing information for the Task Group that would be charged with recommending new guide levels. The Consultation did not specify these methods in detail but recommended that the Task Group should be provided with a sufficiently comprehensive set of analyses to enable the differences in predictions by different models to be reviewed before the choice of a guide value is made.

6.4 Reference Risk

The Consultation agreed with the position taken in the 1984 Guidelines with regard to the choice of 10^{-5} as the level of risk at which the guide value should be calculated, but that the arbitrariness of this assumption should be made still more explicit. This could be done by labelling it as a 'default' assumption, in the way indicated in Section 4.2. The Consultation also discussed the terminology that should be used for this level of risk.

7. EXPOSURE

7.1 Introduction

The subject of exposure is probably the least understood among the technical factors used in the development of guidelines and standards and is often dealt with through simplifying assumptions intended to cover large segments, but not necessarily all, of the population.

Drinking water is rarely, if ever, the sole source of human exposure to the substances for which guidelines have been set. Ideally the guideline concentrations for drinking water would be derived by taking into account total intakes/exposures from air, food and water. Failing to consider total exposures may lead to standards for drinking water that are too slack, or to ones that are overly rigorous in the sense of misdirecting control strategies to less cost effective means.

7.2 Water-related exposures

7.2.1 Consumption of drinking water

The guideline concentrations for organic substances were derived by assuming a daily per capita consumption of two litres of drinking water. Similar figures have been used in the development of recommendations for drinking water quality in Canada and the United States. Previous WHO standards for drinking water have assumed intakes of 2.5 litres per day. The United States also often uses a 10 kg child who consumes 1 litre per day as a basis for certain guidelines or standards.

Comprehensive data on the consumption of drinking water by individuals is scarce. As water intakes are likely to vary with climate, physical activity and culture, the three most extensive studies, which were all conducted in temperate zones, can give only a limited view of consumption patterns throughout the world. In these studies, the average daily per capita consumption was less than 2 litres (1.0 to 1.3 l/day) but there was considerable variation between individuals. In a Canadian study, for example, 12% of the population, aged over 18, consumed more than 2 litres per day, while 2% consumed more than 3.9 litres per day.

The intake per unit weight or surface area is a most important toxicological factor. The Guidelines assume ingestion by a person weighing 70 kg and so the daily fluid intake rate is approximately 30 ml per kg. It is well established that children have greater fluid consumption rates, per unit weight, than adults. In Canada the average consumption rate has been measured at 22 ml per kg per day for adults (18 years +) but at 48 ml per kg per day for 3 to 5 year olds. These figures ignore individual variation and rates in excess of 60 ml per kg per day, twice that assumed by WHO, are easily possible.

Setting guidelines for drinking water by assuming a daily consumption of 2 litres by a 70 kg man does, on average, err on the side of caution. However, it clearly underestimates the consumption of water, and thus exposure, for a substantial portion of the population.

The higher intakes, and hence exposure rates, for children apply for only a limited time but this period may coincide with greater sensitivity to some toxic agents and less for others. Irreversible effects that occurred during early age would have more significant social and public health significance than those that are delayed.

7.2.2 Inhalation and dermal absorption

The drinking water contribution to daily exposure includes direct ingestion as well as some indirect routes such as by inhalation of volatile substances and dermal contact during bathing or showering. In the guidelines, the calculated daily dose was limited to the product of the concentration in micrograms per litre times 2 litres per day assumed ingestion.

The Consultation decided that although empirical data do exist to estimate indirect exposure to volatiles substances from drinking water under some conditions, extending these to a variety of cases would be very hypothetical and would be outside of the scope of these guidelines. Among the variables that would have to be considered are levels of domestic water-use, design of housing, climate, duration of showers and bathing, ventilation rates as well as many others. These kinds of assessment would be within the purview of those responsible for national standards. The science of estimating exposure through dermal contact with highly dilute solutions such as drinking water, is in a much less developed state and would require additional research to develop quantitative estimates.

7.2.3 Organic carcinogens and the fish component

Some of the 1984 guideline values included a factor for consumption of fish which might have bioaccumulated the organic material. The Consultation decided that this factor should be eliminated from revised guidelines because it is highly site specific, and is just one aspect of multimedia exposure.

7.3 Multimedia contributions to total exposure

7.3.1 Introduction

Ideally all standards/guidelines which aim to limit exposures to substance in the environment should be coordinated so that they fully reflect the degree of exposure from other sources. Such an holistic approach would allow the optimal allocation of resources to reduce total exposures and hence minimise the associated risks. Unfortunately this ideal is not possible at present and the best that can be done is to set guidelines for one exposure route by making reference to the total exposure from all sources.

The 1984 guidelines were mostly limited to including non-water contributions in the case of inorganic substances. Guidelines for organic carcinogens were based upon a hypothetical, incremental, lifetime risk contribution. Guidelines for non-carcinogenic organic substances were based upon Acceptable Daily Intake (ADI)-type calculations using an uncertainty factor.

7.3.2 Pesticides

In the case of pesticides in the 1984 Guidelines, some ADI values had been already accounted for by established "tolerance" or "maximum residue limits" for foods. Thus it is possible that some persons in a population might already be receiving a substantial exposure to the pesticide from food intake. The 1984 Guidelines very conservatively allocated 1% of the ADI to drinking water in most cases, which, in effect, supplied an extra safety factor of 100 for most persons on top of the factors used in the ADI calculation.

Some type of arbitrary allocation is probably essential when guidelines are prepared because they must try to cover such a wide variety of complex conditions of exposure. The derivation of national standards from the guidelines should reflect judgement based upon relevant data on pesticide use and dietary patterns.

8. CRITERIA FOR SELECTION

8.1 Introduction

Five criteria were used by the 1980 Leidschendam consultation for selecting groups of compounds and individual compounds for consideration prior to setting the WHO guideline values for organic contaminants. These were:

(a) the existence of evidence that the substances are potentially hazardous;

(b) the concentrations at which the substances are found in drinking water;

(c) the frequency with which the substance or group of substances are encountered in drinking water;

(d) the ease with which the substance or group of substances are measured;

(e) the ease with which the concentration of the substances can be controlled in water.

Compliance with all five criteria was not necessary for inclusion of a compound, nor were the criteria given equal weight. The substances and groups of substances were considered initially in three groupings:

(A) source contaminants;

(B) introduced in treatment;

(C) introduced during distribution.

These groupings broadly reflect different approaches to control. The 1980 consultation took the view that contaminants from group (C) should be regulated by product specifications and these were therefore not considered further.

8.2 Surrogate parameters

The 1980 consultation considered the value of a number of surrogate parameters including total organic carbon, total organic halogen, total organic sulphur, total organic phosphorus, carbon chloroform extract, carbon alcohol extract, organics extractable with chloroform, cholinesterase inhibition and mutagenic screening. As concluded at Leidschendam, some of these were considered to have potential for use in measuring various forms of organic contamination of water, for example in process control, or as research tools. However, as these are group parameters, there are no simple relationships between their levels and possible effects on health. Therefore, they would have limited application in the development of health-related guidelines.

9. ORGANIC COMPOUNDS WHICH NEED CONSIDERATION

9.1 Compounds for which guideline values have been set

The Consultation recommended that all such compounds should be re-evaluated taking into consideration recent toxicological and environmental information, information available from other select groups such as WHO/FAO Joint Meeting of the Committee on Pesticide Residues and changes in the methodology recommended by this Consultation.

It was considered desirable that the following organic substances, including those compounds at present ascribed a "tentative" guideline value, should receive first priority for consideration.

chloroform

carbon tetrachloride

tetrachloroethene

trichloroethene

1,2-dichloroethane

1,1-dichloroethene

2,4,6-trichlorophenol

hexachlorobenzene

gamma HCH

methoxychlor

heptachlor and heptachlor epoxide

aldrin/dieldrin

chlordane

2,4-D

DDT

9.2 Compounds for which no guideline values currently exist

The Consultation recommend that the compounds listed in Table 2 should receive consideration with a view to setting guideline values if appropriate supportive information is available. The four columns in the table correspond to the criteria (a), (b), (c) and (d) as set out in Section 8.1 and modified in Recommendation 10.5 (2).

Table 2.

Compounds, with no guideline value, recommended for consideration

		Health Concern	Concentration	Frequency	Measurement
M	1,1,1-Trichloroethane	V	V	V	V
M	1,2-Dichloroethane	?	V	V	V
H	Vinyl chloride[1]	V	n/a	V	(X)
M	Dichloromethane	?	?	V	V
L	Hexachlorobutadiene	V	?	?	V
H	Bromoform)				
H	Dichlorobromomethane)	V	V	V	V
H	Dibromochloromethane)				
L	Epichlorohydrin[1]	V	n/a	n/a	(X)
H	Chlorination reaction products	V	V	V	(X)
M	Plasticisers diethylhexylphthalate and diethylhexyladipate	V	V	V	?
H	Styrene)	V	?	?	V
H	Toluene)				
H	Xylene)	(X)	V	V	V
H	Ethyl benzene)				
H	Acrylamide[1]	V	V	V	(X)
L	[2]Ethylenediamine tetra-acetic acid (EDTA) Nitrilotriacetic acid (NTA)				
M	Polycyclic aromatic hydrocarbons (PAH)	V	V	V	V
L	Amines[1]	V	?	V	V
PESTICIDES					
H	Atrazine	V	V	V	V
H	Simazine	V	V	V	V
L	Pyrethroids	V	n/a	n/a	V
L	Ethylene dibromide (EDB)	V	V	V	V
L	1,2-Dibromo-3-chloro-propane (DBCP)	V	V	V	V
L	1,3-dichloropropane	V	V	V	V
	1,2-dichloropropane	V	V	V	V
	1,3 dichloropropene	V	V	V	V
L	Aldicarb (sulphoxide and sulphone)	V	V	V	V
L	Carbofuran	V	V	V	?

H, M, L, represent high, medium and low order of priority in review procedure.

[1] Also from water treatment chemicals or material used in water supply.

[2] To be considered with heavy metals as chelating agents.

V = substance satisfies criterion; X = substance does not satisfy criterion; n/a = criterion is not applicable to substance; ? = uncertain.

The usefulness of the total organohalogen determination should be examined with the view of considering its use as a control parameter in water treatment operations.

The trihalomethanes: bromodichloromethane, dibromochloromethane and bromoform, should receive consideration with the objective of setting guideline values for each compound. Consideration should be given to the advantage, or otherwise, of setting a guideline for total trihalomethanes.

Consideration should be given also to those polycyclic aromatic hydrocarbons for which IARC have allocated either a 1 or 2 classification, if such compounds appear frequently in drinking water supplies.

10. CONCLUSIONS AND RECOMMENDATIONS

10.1 Concept and purpose of guidelines

(1) The general philosophy of the 1984 Guidelines remains sound and valid and should not therefore be changed.

(2) The information and assumptions underlying the recommendations could be more explicit so that the intended mode of use of the 1984 Guidelines can be more fully achieved. The Guidelines should, to the degree possible, provide methods and information that are pertinent to their application.

(3) The assumptions made in developing new guidelines should be more evident and their influence explained in such a way that readers can see what the effect of modifying these assumptions would be in terms of water quality and its impact on health.

(4) The revised criteria document should contain a section or an appendix which sets out the rules by which any rounding has been performed, and the text should contain unrounded results, as well, for reference.

10.2 Toxicological considerations

(1) Toxicity data derived from laboratory animals should be selected with careful consideration of species differences in metabolism, pharmacokinetics and sensitivity, to ensure that the conclusions drawn are relevant to man.

(2) Selection of uncertainty factors for calculation of ADI should reflect the quality and extent of the data available as well inter- and intraspecies variation. They should also reflect the severity of the toxic end-point and protect any population sub-groups at particular risk.

(3) When examining data on carcinogenicity, consideration should be given to whether the weight of evidence, including epidemiology, animal studies and genetic toxicology, justifies the use of low-dose extrapolation models.

10.3 Low-dose extrapolation

(1) For those compounds for which the guideline values are to be based on low-dose extrapolation, the results of using different models should be made available to the WHO Task Group charged with determining the new guideline values.

(2) Whatever assumptions and methods are ultimately chosen, they should be fully described and explained in the documentation of the revised guidelines.

(3) The Consultation recommended that, in order to obviate political and semantic arguments, the revised guidelines should avoid the use of the term "acceptable risk" and replace it with the more neutral term "reference risk". This would allow national authorities more freedom to set standards which differ from the guidelines but which are acceptable from the point of view of their own risk/benefit criteria.

10.4 Exposure

10.4.1 Consumption of drinking water

(1) The consumption of 2 litres of drinking water per day by a 70 kg man should be a standard assumption.

(2) The limitations of these assumptions should be made explicit particularly with reference to consumption by children.

(3) Methods to correct for different body weights and water consumptions should be given.

(4) The Consultation concluded that protection of the segment of the population most sensitive to the particular adverse health effect of a contaminant should be the basis for each guideline and that these values should include an adequate margin of safety. However, each national body would need to consider those conditions of exposure that are most relevant to its locality and culture as well as economic and other factors when translating WHO Drinking Water Guidelines into national standards.

10.4.2 Inhalation and dermal absorption

(1) The new guidelines should note the possibility that inhalation and dermal absorption may be significant routes of exposure and, when possible, provide information on estimation methods that can be used by national authorities.

10.4.3 Organic carcinogens and the fish component

(1) Future guidelines should clearly distinguish between exposures that occur via drinking water and those that occur via other water-related routes.

(2) The exposure that occurs via fish in the diet should be excluded from revised guidelines.

10.4.4 The influence of non-water related exposures

(1) For most pesticides the use of a 1% allocation to drinking water should be continued. National standards should contain water allocations based upon more specific local information regarding patterns of pesticide usage and dietary considerations.

(2) Those with responsibility for setting national standards should be aware of the contributions of drinking water to total exposure and take account of the relative significance of the different routes of exposure.

10.5 Criteria for selection

(1) The criteria used by the previous consultation would appear to adequately reflect all the aspects which need to be considered in selecting substances or groups of substances when setting guidelines.

(2) In order to avoid making judgements at this stage on the costs of control of organic contaminants, it would be preferable to replace the word "ease" in criterion (d) by "feasibility" and to omit criterion (e). This would be more in line with the general philosophy of the guidelines.

10.6 Compounds for consideration

(1) The Consultation identified fifteen compounds for which guideline values have been set which should receive priority for re-consideration (Section 9.1).

(2) Twenty-nine further compounds, or determinants, for which there is no guide value were identified for consideration, and twelve of these were assigned high priority (Table 2).

(3) The chlorination by-products, with the exception of the trihalomethanes, are a class of compounds for which the toxicology and analytical chemistry are both undeveloped. This would make it difficult to prepare guidelines for them at present. The Consultation therefore recommended that a 'state of the art' report on these compounds be prepared for WHO by a separate mechanism.

10.7 General recommendations

(1) The Consultation recommends that WHO should give early consideration to reviewing all the parameters included in the 1984 Guidelines, including the microbiological, biological and inorganic parameters. However, highest priority, for review, should be accorded the micro-organic substances.

(2) Because of increasing knowledge and continuing concern, there will be a need for the section of the Guidelines dealing with organic compounds to be reviewed periodically.

(3) The micro-organic substances identified as of high priority in Section 9 of this report should be reviewed with a minimum of delay with a view to the revision or establishment of WHO guideline values for them.

(4) There is a special need for WHO to give attention to the safety of chemicals which enter drinking-water as a consequence of their use in water treatment or in materials used in the supply of drinking-water.

10.8 Recommendations on how the review should be carried out

(1) WHO should make provision for a secretariat to coordinate and oversee the task.

(2) WHO should prepare a document outlining the content of the review papers that would be needed as the basis for a revision of the Guidelines.

(3) WHO should identify those Member States where documents may already exist that would be relevant to the task, and elicit help in preparing other review material as necessary. These documents should be circulated for peer review with particular reference to the completeness of the data.

(4) Within one year of the present Consultation, WHO should convene a task group of toxicologists to evaluate the working documents and recommend guidelines for the two dozen organic compounds of highest priority (these being the compounds for which guidelines or tentative guidelines were previously set, together with the compounds given high priority in Table 2).

(5) A further Consultation including senior scientists of a variety of disciplines should be convened to examine the remaining issues and produce a draft report.

(6) The draft report should be distributed by WHO to the participants for comments and confirmation prior to circulation to identified focal points within the cooperating countries.

(7) The report should then become the basis for a revised guideline document to be published as an addendum to the Guidelines for Drinking Water Quality of 1984.

ANNEX 1

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