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Assessing Health Risks from Environmental Exposure to Chemicals: the Example of Drinking Water

Summary Report of a Workshop Held in May 1998

Organised by the
ILSI Europe Environment and Health Task Force

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ILSI Europe Workshop on Assessing Health Risks from Environmental Exposure to Chemicals: The Example of Drinking Water – Summary Report

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ASSESSING HEALTH RISKS FROM ENVIRONMENTAL EXPOSURE TO CHEMICALS: THE EXAMPLE OF DRINKING WATER

By M. Hofer and L. Shuker

SUMMARY REPORT OF A WORKSHOP HELD IN MAY 1998 IN MUNICH, GERMANY

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BACKGROUND

Organised by the ILSI Europe Environment and Health Task Force, a workshop on "Assessing Health Risks from Environmental Exposure to Chemicals: the Example of Drinking Water" was held in Munich, Germany, from 18 to 20 May 1998. Professor Gerhard Eisenbrand, University of Kaiserslautern (Germany), chaired the workshop. A number of invited experts from academia, the water supply industry and regulatory agencies addressed scientific issues related to drinking water. A major aim was to examine the quality of assumptions and methods employed to estimate potential risks to man resulting from any hazardous substances in drinking water.

Professor Eisenbrand opened the meeting with the observation that water is essential to life and that access to a safe water supply is a basic requirement for human society. In order to provide safe water for human consumption and use, it is clearly essential to identify any hazardous substances in the water supply, to determine what risks they may pose to human health and well-being, and to take appropriate steps to control exposure by setting and maintaining standards.

INTRODUCTORY SESSION

In a paper on "The Epidemiology of Chemical Contaminants of Drinking Water", Dr. Rebecca Calderon, US EPA (USA), reviewed the epidemiology of contaminated drinking water, from the historic study of John Snow in 1856, which was the first to demonstrate a link between cholera incidence and biologically contaminated water, to the correlations observed in the 1970's between certain causes of mortality and water chlorination in the USA. She also discussed susceptible populations and drinking water contaminants as a mixture. Dr. Calderon outlined two examples, namely arsenic and disinfection by-products, and described the unique role epidemiology may have in risk assessment.

Epidemiological studies of drinking water will always address mixtures of agents and are unlikely to be able to identify which specific components of a mixture are causally associated with any adverse effect that might be identified. The power of an epidemiological study is dependent on a number of factors. Of particular relevance to the assessment of human health effects associated with drinking water are the range of exposures, the prevalence of the diseases of interest and the size of the populations studied. Owing to the rarity of relevant cancer end-points and the expectation that, even if there is any effect associated with drinking water, it can lead to only a few extra cancer cases, it seems unlikely that it will ever be possible to establish an association based solely on epidemiological studies between any drinking water contaminant and the induction of cancer.

The need for epidemiologists and toxicologists to work more together is recognized, as is the need for a multidisciplinary approach to producing exposure estimates for epidemiological studies. There is also a strong need to integrate epidemiological studies in the risk assessment process.

EXPOSURE

Dr. Martin Holt, European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC, Belgium), reviewed the "Sources of Chemical Contaminants and Routes into the Freshwater Environment". Drinking water is derived either from surface waters or groundwater. The production, distribution, use and disposal of materials lead almost inevitably to the release of substances either in a localized way or, in many instances, in a widespread manner into water bodies intended to be sources of drinking water. Point discharges are major sources of contamination but can often be dealt with by operational practices and pollution control measures; control of diffuse sources is now becoming, therefore, the major problem.

In a paper on "Water as Consumed and its Impact on the Consumer – Do we Understand the Variables?" Dr. Arnold Bates, Bristol Water plc (UK), described the different sources of drinking water and the corresponding variability in types and amounts of contaminants, water treatment processes, including physical, biological and chemical treatments, and how contaminants can be introduced through the water distribution network. For risk assessment purposes information is needed on water consumption patterns, which may vary depending on temporal, spatial and ethnic factors. The example of Peru showed how restriction of water treatment to protect humans from chlorination by-products led to a serious adverse effect, namely a cholera epidemic. Health officials had misjudged the relative risks of water chlorination and microbial contamination.

Dr. A.M. van Dijk-Looijaard, KIWA (The Netherlands), presented a paper on "Levels of Exposure from Drinking Water", focusing on which compounds should be monitored in drinking water. Monitoring data are needed from the water supply to the tap. For risk assessment purposes the exposure to a substance from drinking water relative to total human exposure has to be addressed. For volatile organic compounds, in particular, exposure routes other than ingestion of drinking water, such as inhalation or percutaneous uptake, must be taken into account.

In a paper on "Predictive Exposure Modelling – A Case Study with a Detergent Surfactant", Dr. Tom Feijtel, Procter & Gamble (Belgium), described models used to predict concentrations of chemical contaminants in the environment, with particular reference to a case study carried out in The Netherlands on predicting the concentration of a detergent in water supplies.

Guidelines and standards

European Union (EU) standards have generally followed the World Health Organization (WHO) guidelines. The current EU drinking water directive covers 62 parameters. In the new proposal, control of 35 of these parameters is still required and 13 new parameters have been added. This gives 48 parameters in total.

An example of changing European legislation, as toxicological understanding has advanced, is the case of fluoranthene. Based on recent toxicological data, fluoranthene has been removed from the suite of PAHs used as the basis for the standard for PAHs in old coal tar linings of water mains. This standard was not based on health, and the presence of fluoranthene, which is one of the most water soluble PAHs, caused numerous breaches of the standard in otherwise excellent waters. Informed risk assessment demonstrated that the levels encountered were not of concern.

Drinking water contaminants and associated monitoring issues

Only a very small proportion of the total number of chemicals that can be found in drinking water is monitored or required to be monitored. There is, therefore, a very limited amount of data on chemicals in drinking water apart from data collected for operational purposes. The requirements for operational monitoring may not be the same as those for risk assessment. For example, most water supply companies will only measure total inorganic compounds for a given element (e.g. arsenic) rather than individual compounds, even though chemical speciation can be of fundamental importance to toxicology.

Appropriate risk assessment could help to identify which chemicals it is most important to monitor in a given water system, so that analytical efforts could be focused on the substances most likely to be present. One approach that has been suggested is to undertake qualitative studies first to ascertain the most likely contaminants of concern followed by quantitative studies as required. A qualitative or semi-quantitative approach to assessing water quality might include the development of effect-based monitoring to quantify mixtures of similarly acting chemicals by, for example, measuring effects on enzyme systems or other possible biological monitors. There is, however, doubt about the usefulness of developing such effect-based monitoring, which could probably only be feasible for concentrated samples.

One group of chemicals about which concern has been expressed is that of pharmaceuticals, which are designed to be active in humans at low levels. However, exposure is normally restricted to clinical use in particular subpopulations. Pharmaceuticals might be one of the priority groups for risk assessment, to determine whether they are of no concern or if further data are required.

In determining how to deal with chemicals of toxicological concern in drinking water, a trade-off may be needed between the presence of a contaminant and further problems arising from its removal. A case in point is the use of ozone (O3) to remove pesticides, which in turn leads to the formation of the more toxic bromate from bromine. Ozone treatment of pesticides could also lead to the production of breakdown products, which may not have been assessed for toxicity. However, since O3 is used in conjunction with granular activated carbon, which removes the lower molecular weight degradation products, this should not present a problem in practice.

Although concerns have been expressed about the potential for chemicals from sewage applied to land or buried in landfills to leach into groundwater, this is not expected to be a major problem, because chemicals in sewage sludge are mainly hydrophobic, having been removed from water by sedimentation in wastewater treatment processes. Thus, such materials can reasonably be expected to stay in soils rather than to migrate into groundwater.

Modelling

Modelling is a powerful tool for assessing exposure, since it can be less expansive than monitoring. However, models do need a robust database, especially on kinetic data. Models also need to take account of factors such as different paths of migration to groundwater and seasonal variations. Predicted environmental concentrations (PEC), determined by modelling, are dependent on in-stream removal rates, physicochemical properties, sorption and sedimentation. For volatile compounds, volatilisation and biodegradation are the most important determinants of removal in the aquatic environment.

Only for a relatively small number of chemicals in drinking water have good dose-response relationships been established. Otherwise, models and extrapolations from high dose to low dose, and from animals to humans have had to be used for risk assessment. More dose-response data would facilitate better risk assessment and hence influence better ultimate risk management.

Risk assessment and risk management

At the interface between risk assessment and risk management, it is worth noting that small differences in interpretation of toxicological data may have a big impact on the feasibility and cost-effectiveness of control. In risk management, consideration must be given to pursuing the most effective strategies; for example, in the case of lead exposure, will a reduction in drinking water standards from 20 to 10 µg/litre be more or less cost-effective in protecting man than a further reduction of lead in petrol?

A system in which risk assessment decisions are based solely on scientific judgement, and are made independently of any possible risk management decisions, is reasonable and is to be supported. None the less, to assist risk management, risk assessment, though made independently, should indicate the limitations and uncertainties inherent in a given decision. With better risk assessment and risk prediction, risk managers will be able to make more informed decisions. Despite the independent decision-making processes used in risk assessment, risk management and policy and regulation, a more iterative approach is to be encouraged. Risk management has to balance risk and benefit. A case in point is the issue of water chlorination, where the benefits that accrue to a given population will be assessed in the population that is at risk.

Whether there is sound scientific evidence for an adverse human health effect, or only an indication of a possible effect, regulators have to make decisions, and this is the rationale for the use of some form of precautionary principle. Often some sort of control or prevention cannot be avoided simply on the basis of insufficient data.

However, the precautionary principle must itself be applied with caution. A situation such as that in Peru, where an ill-advised decision to reduce water chlorination because of fears of potential carcinogenicity from total halogenated methanes (THMs) led to an outbreak of cholera, which affected tens of thousands and killed thousands, and extended into other Central and South American countries, should not be allowed to happen again.

THE RISK ASSESSMENT PROCESS

In a paper on "Safe Drinking Water: the Toxicologist's Approach", Dr. F.X. Rolaf van Leeuwen, WHO European Centre for Environment and Health (The Netherlands), reviewed, with examples, the linearized multistage model for genotoxic carcinogens and the threshold model for other toxicants used by WHO in setting drinking water guidelines. He also discussed the use of newer techniques such as physiologically-based pharmacokinetic (PBPK) modelling and benchmarking.

In considering "Measuring Risks in Humans: the Promise and Practice of Epidemiology", Dr. Calderon, US EPA (USA), compared the relative advantages and disadvantages of epidemiological risk assessment and quantitative risk assessment and recommended the use of epidemiological studies to evaluate the outcome of risk management decisions.

Dr. John P. Groten from TNO Nutrition and Food Research Institute (The Netherlands) addressed "Mixtures and Interactions" in his presentation, describing the problems associated with evaluating mixtures of chemicals, potentially a major difficulty in evaluating drinking water contamination.

Models for risk assessment

In commenting on the "traditions" linearized multistage quantitative risk assessment model used for genotoxic carcinogens, and on risk assessment based on the threshold model used to determine tolerable daily intakes (TDIs) for other toxicants, both methods used by WHO for drinking water contaminants, it was apparent that little consideration has been given to new techniques, such as the benchmark approach and PBPK models. These newer techniques are beginning to find a place in risk assessment.

The endpoints most often used for toxicological assessment relate to traditional target organ toxicity (e.g. pathological changes in the liver or kidney). In future risk assessments, perhaps more consideration should be given to more subtle endpoints, such as immunotoxicity and endocrine effects. Indeed recent guidelines from the Organization for Economic Cooperation and Development (OECD) have been changed to reflect the need to evaluate immune system effects.

Chloroform has recently been reassessed in the USA, using the threshold approach, because there is now good evidence that it is not a genotoxic carcinogen. Not all agencies follow the same approach, and this can cause significant confusion over the standards for chemicals such as chloroform. Attempts are therefore being made to harmonize approaches to risk assessment. Part of a more unified approach may include the use of both PBPK models and the benchmark concept.

A question to consider is whether a different approach to risk assessment is needed for low-level contaminants. For example, although bromate is an oxidizing agent (therefore its presence in water might be taken to indicate a toxicological risk via that mechanism), its redox potential at the levels found in drinking water is so low that it will not effectively act as an oxidant.

Allocation factors

The current default assumption is that, in the absence of any data to the contrary, 10% of total daily intake of a chemical comes from drinking water. The remainder comes from other sources, including air and the diet. This 10% allocation factor will be used in determining a TDI for a chemical from drinking water.

No allowance is made for exposure from other sources in setting standards based on the risks for chemicals calculated using the linearized multistage model. This may be unhelpful to risk managers. However, there are inherent weaknesses and uncertainties in any mathematical model. Therefore, the degrees of uncertainty as well as the risk assessment itself should both be known to the risk manager and policy maker; risk assessment decisions and the reasons for making them and any default assumptions used should be transparent.

Relevance of epidemiological and experimental toxicology studies for risk assessment

An often supposed limitation of epidemiology studies is that they cannot reliably detect increased risks of less than 20%. However, it may be reasonable to suppose that this is an acceptable limitation, since when investigating cause and effect it is often the case that the cause may be multifactorial, even though one cause may be responsible for a major part of the increase in risk. Furthermore, even a very low increase in risk, such as a 2% increase, may be easy to detect for a very prevalent disorder, such as an infectious disease.

A good epidemiological study could provide the data to reduce the uncertainty factor in the TDI approach by a factor of 10. Although one strength of epidemiology is that it is based on real human populations, including susceptible groups, the response of susceptible groups may be averaged out.

The contribution of epidemiological data to risk assessment increases in parallel with increasing toxicological data and information about mechanisms of action. Epidemiological studies can be made more rigorous through better design as more becomes known about mechanisms. The issue of what it takes to establish “no effect” in an epidemiological study is still controversial. Lack of evidence of an effect is not the same as evidence of the lack of an effect.

The power of an experimental study in establishing a good dose-response relationship, particularly at the low doses encountered in the environment, is not necessarily any greater than the power of a well designed and well conducted epidemiological study.

Mixtures and interactions

Although it is recognized that in summing the effects of mixtures of chemicals it would be preferable to use a lowest-observed-adverse-effect level (LOAEL), or other measure such as the benchmark dose which is less dependent on experimental design, rather than a no-observed-adverse-effect level (NOAEL), in practice toxicity testing protocols (three dose levels in a 4-week study) do not permit the accurate determination of a LOAEL.

For some classes of chemicals in drinking water, although interactions might theoretically be possible, in practice they will be unlikely since the substances of concern will be extremely dilute.

Additivity may refer to dose or response. For example, although there will be no dose additivity between a non-toxic chemical that facilitates transport through the skin and a second toxic chemical, the toxic effect of the latter chemical may be enhanced because of increased penetration.

Uncertainties inherent in risk assessment

Although the separation of the risk assessment process from the risk management process may represent the ideal, there is at least a perception that toxicologists making risk assessments are likely to be influenced by factors other than the strictly scientific, and may tend towards the use of higher uncertainty factors to ensure a higher degree of safety.

Risk management may be influenced by public opinion and media reporting. Changes in policy may sometimes be dictated more by societal pressures than by good scientific judgement. Such influences should not be allowed to impact on risk assessment, which can only meaningfully be based on sound scientific judgement and not on ethical, economic or other such factors. The precautionary principle should not influence risk assessment.

CASE STUDIES

In a paper on "Public Health Implications of New Guidelines for Lead in Drinking Water: A Case Study in an Area with Historically High Water Lead Levels", Dr. Graham Watt, University of Glasgow (UK), discussed the rationale for measures to reduce blood lead levels further, although it is recognized that the decreased risk to the individual associated with any further reduction will be very small. The advantages that further reductions in blood lead levels will incur relative to the disadvantages associated with other causes of low intelligent quotient (IQ), such as socio-economic factors, are questionable. Although chemical water treatment measures have been effective in contributing to the reduction of mean blood lead levels in the European population, there are still hotspots-houses in which water lead levels are very high. New methodologies will have to be developed to identify and manage these remaining high-risk properties.

"Clues and Uncertainties in the Risk Assessment of Arsenic in Drinking Water" was the title of the presentation by Dr. Jean-Pierre Buchet, Catholic University of Louvain (Belgium). There are considered to be several limitations to the Taiwanese data set previously used to establish guideline values for arsenic. Further factors that may have affected the cancer outcome in Taiwan are low protein levels in the diet and the role of UV radiation, which may have been a co-factor in the genesis of skin cancer. The latter may explain why it has not been possible to repeat the findings from the Taiwanese study in more northern countries. Skin cancer is not the only endpoint of concern. Reports from Taiwan and China and from a small study in the USA suggest that arsenic may also be implicated in cardiovascular disease.

It is recognized that risk assessments for arsenic may need to take into account the fact that it may be also an essential element, the growth of animals fed arsenic-deficient diets is impaired. However, it is not easy to induce a single element dietary deficiency, and other essential minerals may also be implicated in these studies. Nevertheless, on the basis of studies conducted, the daily requirement of arsenic to prevent growth retardation is less than the dose implicated in carcinogenesis.

Dr. Maged Younes, WHO International Programme on Chemical Safety (IPCS, Switzerland), talked about "Pesticides in Drinking Water – A Case Study". As many individual pesticides are currently in use and for many of them few toxicological data are available, a precautionary approach has been adopted, and drinking water standards have been established for pesticides as a group.

One of the biggest problems faced by water suppliers is the short-term presence of a high concentration of a pesticide in drinking water. The precautionary principle may also apply here. If, for example, an individual pesticide is found in drinking water at a level higher than the standard, a decision has to be made as to whether the greater risk is the presence of the pesticide in the water supply or turning off the water supply. The WHO/FAO Joint Meeting on Pesticides Residues (JMPR) is currently evaluating guidance to be given in such instances.

The presentation of Mr John Fawell from WRc National Centre for Environmental Toxicology (UK) was a "Risk Assessment Case Study – Chloroform and Related Substances". Exposure to volatile compounds such as THMs, which arise as by-products of chlorination, is likely to be as great through routes such as showering as through drinking water; recent evidence suggests that taking a shower can double exposure to chloroform. Associations have been observed between consumption of THMs and various cancers and reproductive effects, but the associations are only weak to moderate. For effects such as cancer, with long latency periods, the lack of good early data on THM concentrations and the fact that concentrations have reduced over time make the determination of a causal relationship unlikely. Mechanistic data on THMs have been limited, but are improving and do not support a plausible biological mechanism for the epidemiological findings. In contrast the data clearly demonstrate a risk for consumption of microbiologically contaminated water. In the UK, before the 1970's, there were 12 infections disease outbreaks associated with the water supply, of these 10 were associated with a failure of chlorination.

Dr. Paul M.D. Foster, Chemical Industry Institute of Toxicology (CIIT, USA), presented "Effects of Di-*n*-butyl Phthalate (DBP) on Male Reproductive Development in the Rat: Implications for Human Risk Assessment". The studies on DBP demonstrate the need for multigeneration studies to detect non-receptor-mediated anti-androgenic effects. There is clearly a spectrum of possible mechanisms leading to similar effects. For example, flutamide is a classic androgen receptor antagonist, vinclozolin is anti-androgenic and DBP is anti-androgenic but with no evidence for receptor-mediated activity. Only multigeneration studies, not classical teratology studies, will demonstrate such effects. This suggests there may be a need for a revision in testing protocols.

Despite current concerns about endocrine disrupting chemicals (EDCs), it is not clear that drinking water is likely to be a major source. Many EDCs are hydrophobic and therefore, if present in raw waters, can be relatively easily removed by treatment. Even alkylphenols, which are more water soluble, are fairly rapidly absorbed onto sediments.

RISK EVALUATION LEADING TO STANDARDS SETTING – WORKING GROUPS

Toxicants arising from water processing

The water industry uses a number of physical and chemical treatment barriers, including coagulants, flocculants, disinfectants, oxidants and softening agents, NaOH and ion exchange resins for nitrate and sulfate control, acids and alkalis for ph-control and alkali and phosphate for metal solvency control, to treat surface and ground-waters to make them suitable for human consumption. Other chemicals, such as PAHs, epoxyresins, phthalates and monomers, may leach into drinking water from the distribution network and in some regions fluoride may be added to drinking water supplies to improve dental hygiene. Possible new physical treatment techniques include hyper-, nano- and ultra-filtration and high-intensity light irradiation. There is likely to be an increasing need to re-use water, in particular to cope with seasonal shortages; none the less new treatment techniques should be capable of producing good quality recycled water.

The major priority is to safeguard the microbiological purity of drinking water and, though disinfection techniques will lead to the presence of potentially toxic by-products, as stated by WHO, "efficient disinfection should never be compromised for the sake of eliminating disinfection by-products".

Levels of disinfection by-products can be controlled by ensuring good quality raw water, reducing the turbidity of raw waters, minimizing the use of disinfectants/oxidants, and pre-chlorination and ceasing to use break point chlorination.

In considering toxicants arising from water processing, there may be circumstances in which the relative risks of chemicals arising from such processes may have to be balanced. For example, oxidants may be used to remove pesticides, but may also result in the formation of bromate, NaOH may be used to increase pH and soften water and so reduce metal solvency, and the increase in sodium concentration has to be balanced against reductions in, for example, copper and lead concentrations at the tap.

Distribution of drinking water also influences the presence of toxicants in the water supply. For example, total THMs can increase by 10-400% in the distribution network and other chemicals may leach from distribution materials, in particular, there are only limited data on what leaching takes place from ageing materials.

Source protection is one of the most effective ways of reducing the potential for introducing toxicants into raw water. Collaborations with the relevant agencies to protect river basins and with the agricultural sector to protect groundwaters and cooperative covenants with industry have all been effective in certain circumstances in helping to protect the quality of raw waters. For example, discussions with farmers in The Netherlands and France, public education programmes in Dutch cities to advise on the use and disposal of household and garden products, official covenants with industries in Belgium, and long-standing cooperative agreements for users of the River Rhine have all had some benefits. Catchment control is one of the strategies of the new EU Framework Directive.

Inorganic contaminants

Several factors, including speciation, the nutritionally essential nature of sonic inorganic chemicals, accumulation and the availability of human data, may all affect the risk assessment of inorganic contaminants in drinking water.

Speciation will affect toxicity, different oxidation states of the same element may have very different toxicity, bioavailability and metabolism.

Several elements are nutritionally essential, which means that they show a U-shaped dose-response curve and that large uncertainty factors cannot be used in risk assessment calculations. In some cases (e.g. fluoride) there may be a narrow window of safety between a nutritionally essential dose and a toxic dose. For those essential elements, a range of acceptable intakes, rather than a safe level, should be established.

Accumulation of inorganic compounds is another important factor for risk assessment, data on chronic effects must be incorporated into the risk assessment, and uncertainty factors may need to be applied to account for the nature or severity of adverse health impacts.

Some inorganic contaminants may interact with each other even at the low levels found in drinking water; the bioavailability of copper will, for example, depend on the copper/zinc ratio.

In recent years concerns over organic contaminants in drinking water have tended to overshadow potential problems associated with inorganic contaminants. However, it is recognized that inorganic contaminants are often present at higher concentrations and may cause greater difficulties for treatment. The risks associated with certain inorganic contaminants at the levels found in some drinking waters may be greater than those for most organic contaminants. For the future it may be beneficial to direct more research towards inorganic rather than organic drinking water contaminants.

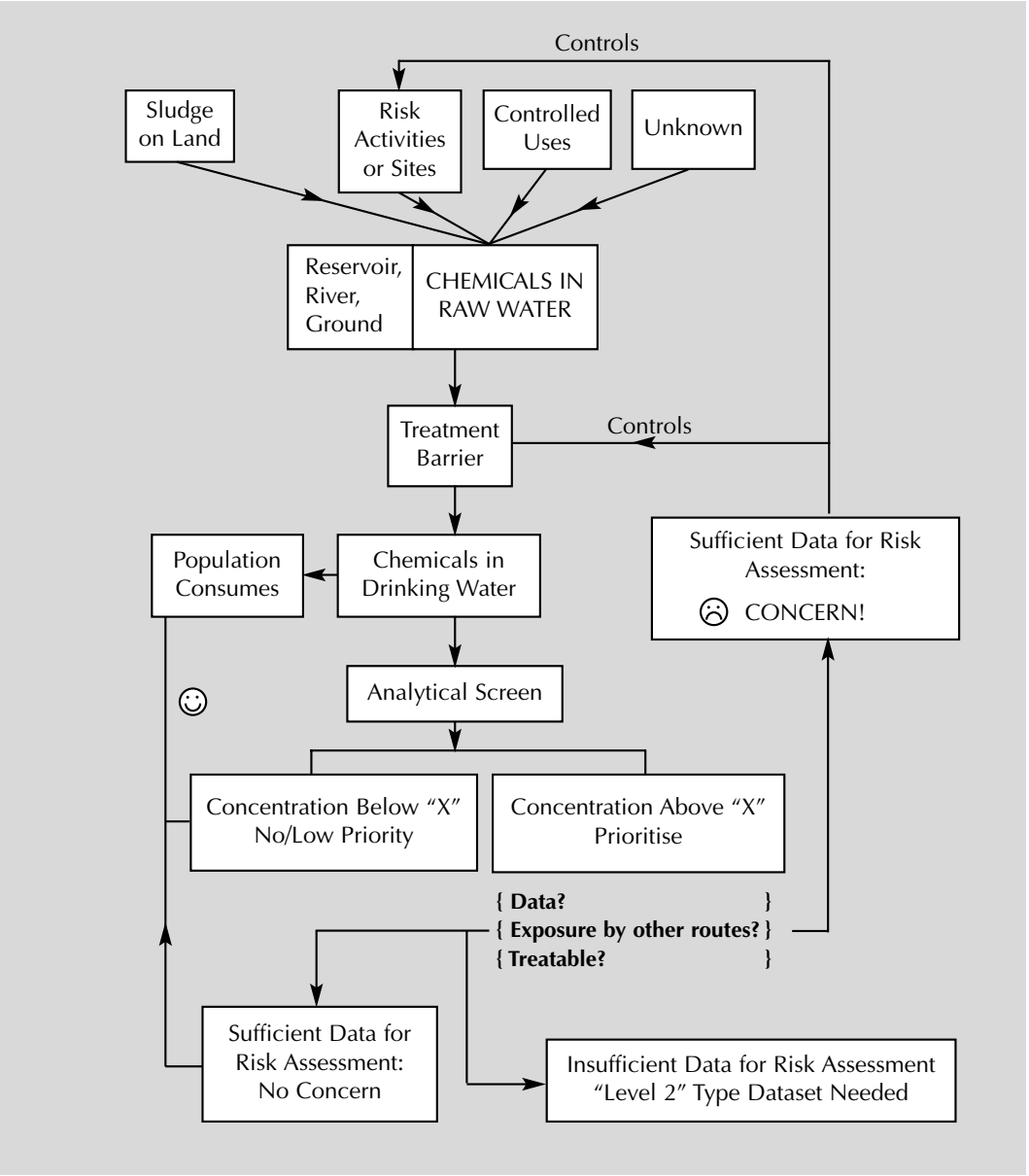
Man-made organic chemicals

It is now possible to detect many hundreds of man-made organic contaminants in drinking water. These may arise from many sources including application of sewage sludge, agricultural application of pesticides and fertilizers, household chemicals, run-off from highways, industrial point sources, contaminated land sites, industrial effluents and sewage treatment.

A first task in dealing with risk assessment of man-made organic contaminants is therefore to decide how to prioritise such contaminants for risk assessment. Two complementary approaches could be used to facilitate such prioritisation. One approach is locally driven and would take account of data pertaining to chemicals found in water supplies and knowledge of local conditions (e.g. industry, urbanisation, agriculture, etc.) likely to lead to particular contamination, such an approach would also take into account degradation products and, for example, contaminants formed by interaction of water treatment chemicals with chemicals in raw waters. A second approach would be to consider available data on individual chemicals generated by EU directives on new chemicals, existing chemicals, high production volume chemicals and so on.

A scheme summarizing potential sources of man-made organic contaminants and a possible framework for prioritising risk assessment is presented in Figure 1.

Figure 1. Potential sources of man-made organic contaminants and possible framework for prioritising risk assessment



According to this scheme, a scientific judgement would be made as to what level of contamination in drinking water represents a threshold of toxicological concern, and any contaminants found below such a threshold level would be considered to have low priority for risk assessment or monitoring. Such an approach would leave a manageable number of chemicals for further consideration. The large number of pesticides found in raw waters would be unlikely to remain as priority chemicals under such a scheme since they are generally present at such low levels.

Even though using such a framework would reduce the number of chemicals to be prioritised for risk assessment and control, there are still likely to be a number of contaminants for which toxicological data are currently lacking. Until the required toxicological studies have been performed it will be necessary to adopt a conservative approach to standard setting for such chemicals, which could prove to be an expensive option in some cases.

Nevertheless, experience has already shown that, particularly in the case of the temporary presence of a man-made organic contaminant with little known toxicity, immediate measures to reduce or remove the contaminant may be the most practical immediate short-term response. Short-term problems, especially concerning temporarily high levels of contaminants, may require rapid decision making, and the exchange of experience between water suppliers by sharing of monitoring and toxicological databases, as is done in the UK, might facilitate such decisions.

Naturally occurring chemicals in drinking water

Naturally occurring chemicals include some of the inorganic chemicals considered above, as well as algal toxins and microbial metabolites. Intervention to remove naturally occurring chemicals is largely only achievable at water treatment plants, although algal toxins can be controlled by controlling algal growth in lakes and reservoirs.

For naturally occurring chemicals, it is particularly important to consider exposure from sources other than drinking water; for example, other sources of exposure by ingestion may include vegetables. Levels of contaminants in drinking water should be considered in relation to levels of the same substances in other environmental compartments. If there is a large population exposure to the substance at levels much greater than those found in drinking water, with no apparent adverse effect, then there is little need to be concerned about drinking water as a source of exposure.

The regional variability in water and food consumption has implications for attempts to make risk management decisions that will be equally applicable across a large geographical region with wide cultural differences. More information is needed on food and water consumption patterns throughout the European region. Some data are expected from the current European Prospective Investigation on Cancer and Nutrition (EPIC) study. Natural and temporal variations in the occurrence of toxicants will also affect exposure, for example, algal toxins will only occur when algae bloom, and inorganic contaminants will vary with geological formations. Another factor that varies widely across Europe is the use of private wells instead of public water supplies. Private wells are far more vulnerable to contamination by naturally occurring compounds like arsenic and nitrate.

Margin of safety

The principal use of the results of toxicity tests on drinking water contaminants is to assess the potential risk to human health, taking into account various assumptions about exposure and susceptibility.

Risk assessment is a scientific exercise and the strength of a risk assessment will be enhanced by several factors such as knowledge about kinetics, mechanisms of action, dose-response relationships, susceptible groups in the population, and use of appropriate endpoints and scientifically justifiable uncertainty factors in the risk assessment process.

Risk management follows on from risk assessment, and while use of the precautionary principle is recognized as being valid in risk management, it should not influence risk assessment. The precautionary principle will be applied, in particular, in situations where failure to act cannot be justified by lack of relevant data.

At the end of the process, from hazard identification through quantitative risk assessment to risk management, the risk manager needs to know and be able to communicate what margin of safety there is between an expected or estimated exposure and the NOAEL (or LOAEL) derived from toxicity studies. The nature of the expected effect, that is acute, chronic, or delayed, will influence what is considered to be an acceptable margin of safety. It should be emphasized that the margin of safety is not, as is often mistakenly communicated, the difference between an estimated exposure level and the TDI, nor is it a "safety factor" built into the standard setting exercise.

The margin of safety can be used as part of a screen for priority setting. If there is a wide margin of safety between an expected or estimated exposure and the NOAEL, then there is little need for the introduction of additional control measures or more toxicity testing.

OVERALL DISCUSSION

Acceptable risks

Although the estimation of risk is essentially a scientific process, determination of an acceptable level of risk is a risk management decision. Within the EU, the Ethics Committee of DG XXIV is currently debating what an acceptable risk level should be for the European region.

Presenting risk levels as risk ranges is one option. For genotoxic carcinogens, risk ranges can be presented as concentrations corresponding to an excess lifetime cancer risk of, for instance, 10^{-4}, 10^{-5} or 10^{-6}. However, the EPA risk assessments, for example, are currently moving away from only estimating lifetime risks, and are moving towards more narrative descriptions of risk. For compounds with a threshold for effect, dose-response information or percentile of affected population could be used to establish risk ranges.

Presenting risk assessment and risk management decisions in an acceptable and transparent fashion is an ongoing problem. Clarity in communication will be enhanced by a consistent use and understanding of terms such as uncertainty factor, safety factor and margin of safety by scientists, risk managers, policy makers and regulators alike. Additional efforts should be made to present in a clear and concise way how a risk assessment has been arrived at (including what uncertainty factors were required and how they were determined), how and why the precautionary principle may or may not have been applied in risk management, and what additional uncertainty factors (for example to allow for severity of effect) were required for risk management.

Standards, monitoring and compliance

As specified in the proposed EU Directive, only health-related standards should be regulated. In addition to the basic health-related standards covered by EU Directives, additional standards may also be required on a local or regional basis, as dictated by local needs and conditions. For example, depending on local geological formations it may be necessary to introduce additional standards for arsenic, or local chemical production may require additional standards for chlorophenols. EDCs are also possible candidates for future European legislation.

Standards should not be based on the limit of detection (i.e. virtual zero), since detection limits may change considerably over time as newer, more sensitive techniques are introduced. Analytical methods should be appropriate to the needs. In the absence of sound scientific data to support a standard, either a precautionary approach should be adopted to set an absolute value for a default standard, and the basis for the decision should be made transparent, or no standard should be set at all. Standards should be reviewed as new data are generated.

Although there appears to be a lack of published or generally available monitoring data on levels of toxicants, such as THMs and DBPs in drinking water, it is recognized that water suppliers themselves have extensive databases developed from monitoring data, collected for compliance purposes. It is recommended that moves should be made to share these and make them more widely available. In particular, a wider availability of databases across Europe may be especially useful in crisis management situations.

An iterative approach should be taken to data collection. Levels of a specific contaminant in a water supply close to a default standard (established based on a precautionary approach adopted in the light of a lack of scientific data) should be a trigger to generate further data to confirm or modify the standard. Conversely, if levels in drinking water are substantially below the default standard there is little need for further monitoring and control.

The location of samples for screening purposes depends on the likely source of the contamination. For example, samples for lead, which comes from service connections and plumbing in buildings, should be collected at the tap, whereas raw water contaminants from diffuse sources, such as nitrates or arsenic, should be monitored at the treatment plant.

Exceeding non-biological parameters should be permitted on a case-by-case basis, and what is permitted should be decided by regional or national health authorities, again depending on local needs and conditions. Temporary excursions above safety standards may be of less importance for contaminants causing chronic effects than for those causing acute toxicity.

Adequacy of data

It is often the case that the available toxicological or exposure databases are not entirely sufficient for ideal risk assessment so that risk assessment and subsequent risk management decisions may sometimes have to be based on an incomplete data set. Factors that might be considered as triggers indicating the need for further review or additional data collection include new experimental or epidemiological studies, identification of additional adverse health endpoints of concern, indication that an element is essential, and costs of measures to reduce contamination.

There is a paucity of good epidemiological data to assess the effects of drinking water contaminants. This means there has been a heavy reliance on animal data for risk assessment purposes, although to support future risk assessment increased use of epidemiological studies should be explored. The reliance on animal data highlights both the importance of assessing the relevance of effects observed in animals to predict outcomes in humans, and the need to investigate possible differences in kinetics, metabolism and in mechanism of action between humans and experimental animals.

Models for risk assessment

To set safe levels of exposure or guidance levels for drinking water contaminants it is recommended that human data, if available, should be used and all potential adverse health effects should be taken into account in the risk assessment process. Exposure monitoring is recommended to ensure the quality of intake data.

A threshold approach to risk assessment should be used for inorganic contaminants. The linearized multistage model for risk assessment is not applicable to inorganic drinking water contaminants since none of them are genotoxic carcinogens. Using the threshold approach, uncertainty factors can be applied, as appropriate, to allow for factors such as individual variation, inadequacies in the database and the fact that a toxicological endpoint used to derive a TDI may not be the only endpoint of concern; some weighting should also be applied to take into account any potential for delayed, severe toxicity. In the absence of toxicological data to justify a specific value for a given uncertainty factor, accepted default values should be used. However, there are sometimes inconsistencies, both in the values of the uncertainty factors used and in their application. More efforts could be made to encourage consistency in approaches to standard

setting and to ensure that clear justifications are given when deviations in approaches are adopted. More use should be made, in future, of retrospective analyses to evaluate the numerical values of the uncertainty factors used.

It is recommended that, although uncertainty factors based on scientific considerations such as factors to account for individual variation or inadequacies in the database, should be included in the risk assessment process, extra uncertainty factors introduced to allow for the nature or severity of an effect should be applied only at the later risk management stage. In this way it should be easier to separate those factors addressing scientific uncertainty (risk assessment) and those belonging to risk management arising from application of the precautionary principle. The process leading to risk management should, therefore, become more transparent. Risk managers should be aware of the whole risk assessment process and how any uncertainty factors have been taken into account during the process, and they should be able to communicate such information to the consumer.

Particularly for essential elements there may be a fine balance between risk and benefit, and it may often be advantageous to consider what additional data might be generated in order to modify default uncertainty factors, such that they can be minimized as far as is toxicologically justifiable. More detailed knowledge on mechanisms of action, coupled with more precise and focused monitoring of toxicological endpoints will allow more accurate inter-individual and inter-species extrapolation of data.

The TDI approach to risk assessment for drinking water contaminants also includes a factor to allow for all possible routes of exposure, thus an allocation of the proportion of total intake to drinking water is applied.

The concept of threshold of toxicological concern has already been applied to flavours and food packaging materials. This may be a particularly important concept to develop in order to facilitate progress in risk assessment for drinking water contaminants.

Susceptible groups

Some drinking water contaminants may present particular risks to susceptible groups within the general population. Pregnant women and infants, for example, are susceptible to the toxic effects of lead; patients with kidney disease may be affected by aluminium in drinking water; arsenic may have an effect on people with compromised nutritional status, and genetic polymorphism may affect responses to some organic and inorganic contaminants.

In the risk assessment process, differences in susceptibility will usually be accounted for by the use of appropriate uncertainty factors. However, if a particular subset of the population is identified as being more susceptible to a drinking water contaminant or group of contaminants, the risk assessment process should concentrate on these groups where appropriate.

GENERAL CONCLUSIONS

Protection of the water sources is one of the most effective ways of reducing the potential for introducing toxicants into the water supply. Although the major goal for drinking water is to provide safe water for human consumption, it is recognised that the environmental impact of water treatment and water distribution must also be considered. While it is recognised that in many cases epidemiological and toxicological data may be insufficient for the ideal risk assessment processes, none the less a framework is needed to enable sensible judgements to be made in the short to medium term, either while relevant data are being generated, or as a pragmatic course of action when the generation of more data is not justifiable. All available relevant scientific data should be used in making a risk assessment, and the limitations and uncertainties in the scientific data and judgements used in any risk assessment should be presented in a clear and unambiguous way to the risk managers, policy makers and regulators.

A clear example of a concept that is potentially understood differently by toxicologists and risk managers is that of "margin of safety". The meeting proposed that a new concept "margin of protection" be used by risk managers to represent the combination of uncertainty factors and extrapolations used in setting standards and hence the margin between a given standard and the lowest lever at which an adverse effect might be expected.

While it is important to be able to make rapid or interim risk assessment decisions in some circumstances, it is also important to guard against precipitous decisions, which may later prove unwarranted or erroneous. For example, despite considerable public and political interest in EDCs and although experimental studies have demonstrated adverse effects at very low levels, the human health implications are still effectively unknown.

The threshold model for non-genotoxic carcinogens and other toxicants provides a basic framework for risk assessment for drinking water contaminants. Agreed default values for uncertainty factors and for apportionment of intake to drinking water can be applied to experimentally determined NOAELs and to ADIs, respectively. Where available, additional toxicity or mechanistic data can be used to modify the default values.

Risk assessment procedures for genotoxic carcinogens are currently being re-evaluated, and the US EPA, for example, has recently modified its approach to allow more explanatory narrative to accompany lifetime risk estimates.

Many databases have been generated within the water supply industry, both of chemicals monitored for operational reasons and of chemicals unexpectedly encountered at short-term high-level peak concentrations, which had to be controlled immediately. Measures should be encouraged to combine such databases, to provide the resources to maintain them and assure the quality and validity of the data included, and to make them widely available across Europe to the water supply industry and to agencies and regional authorities undertaking risk assessments for drinking water contaminants.

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