EFFECTS OF DISINFECTANTS ON ORGANIC SUBSTANCES IN WATER - BALANCING CHEMICAL AND MICROBIAL RISKS

Report to the Department of the Environment
EFFECTS OF DISINFECTANTS ON ORGANIC SUBSTANCES IN WATER - BALANCING CHEMICAL AND MICROBIAL RISKS

Report to the Department of Environment

Report No: DWI 3904/1
August 1995
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Contract Manager: J Hutchison
Contract No: 09005
DoE Reference No: PECD 7/7/137
Contract Duration: 1 October 1984 to 31 March 1995

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EFFECTS OF DISINFECTANTS ON ORGANIC SUBSTANCES IN WATER - BALANCING CHEMICAL AND MICROBIAL RISKS

EXECUTIVE SUMMARY

This is a stand-alone report commissioned under the Department of the Environment’s contract Effects of Disinfectants on Organic Substances in Water (Reference No. PECD 7/7/137). It specifically examines the USEPA’s recent approaches to modelling the formation of disinfection by-products in drinking water and attempts to balance the risks of infectious disease with those of cancer from by-products.

The first part of the report reviews the features of microbial disease and infectivity, the kinetics of the disinfection process, the formation of by-products by different disinfectants, the features of carcinogenicity and derivation of standards for by-products and the frameworks for legislation and guidelines adopted by the USEPA, the UK, the European Union and the World Health Organisation.

The features of the modelling carried out by the USEPA are then considered in detail, the results described and their validity critically assessed. The successive interacting parts of the model calculate reduction in microbial risks from treatment and disinfection, the generation of by-products from precursors in raw water, having selected the cheaper option of disinfectant and provide risk estimates. Unfortunately, the underlying relationships between dose and risk, the quality of source water and the assumptions made are all variable or uncertain so that the output is both imprecise and inaccurate and cannot be calibrated. The value of the model is therefore qualitative and is set against there being little convincing evidence that drinking-water contaminants are a significant cause of human cancer. The modelling activity is therefore seen to be regulation-driven. No consistent balancing of chemical and microbiological risks can be achieved, except for individual pairs of pathogen and by-product.

The approaches used by the USEPA are seen to be irrelevant to the needs of the UK's regulators (i.e. the Department). Alternative approaches are suggested. One study, already underway will attempt to find more reliable baseline data, relevant to UK conditions and use uncertainty analysis with statistical distributions appropriate to water supply. A prudent course, is to consider the reduction of by-products by attention to treatment prior to terminal disinfection, thereby improving the efficiency of disinfection, as well as reducing the formation of by-products. Other recommendations are to investigate the safety factor inherent in the requirement for absence of Escherichia coli in drinking water, examining the cost-benefit relationships of disinfection and other barriers to transmission of infection and exploring the public’s perception of microbial and chemical risks from drinking water against other environmental hazards.

The views expressed in this report are those of the author and not necessarily those of the Department of the Environment or any other government department or organisation.
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1. BACKGROUND TO THE PROJECT

A large number of chemicals are produced at low concentrations during chlorination of drinking water. However, other oxidants/disinfectants which could be used to replace chlorine, also result in by-product formation, but less is known about their identities and health effects. Substances, such as pesticides and water treatment chemicals, can also react with chlorine and ozone to produce by-products, most of which have not been evaluated.

There is a trend in some European countries to avoid the use of chlorine in order to avoid the formation of undesirable by-products. New legislation on disinfection by-products (DBPs) is under consideration in the US and a revision of the EC Drinking Water Directive (80/778/EEC) has been issued in draft form by the European Commission. A key feature of the EC revision is the specification of parametric values for the DBPs bromate (10 µg l⁻¹), bromodichloromethane (15 µg l⁻¹) and chloroform (40 µg l⁻¹), with the qualification that the last two are to be measured at the outlet of the water treatment plant and that, where necessary, the parametric value for bromodichloromethane can be increased to 25 µg l⁻¹, if that for chloroform is reduced to 30 µg l⁻¹. Some of these values could be exceeded in UK water supplies if these values are adopted. The WHO Guidelines for Drinking Water Quality (WHO 1993) set guidelines for a wide range of DBPs. More information is required on the possible implications of the WHO guidelines and on the identity and health effects of by-products from reactions of alternative disinfectants with organic substances and treatment chemicals. Models for DBPs formation and relative chemical and microbiological risks are being developed in the US by the EPA. Similar models for the UK situation need to be evaluated.
2. **OBJECTIVES AND PROGRAMME OF WORK**

The objectives of the whole project are:

To study the effects of disinfection of water by chlorine or ozone on a range of selected organic substances likely to occur as contaminants in water.

To identify products of these reactions.

To identify the by-products formed by the action of water treatment disinfectants on chemicals used in water treatment.

To assess the occurrence of trichloroacetic acid and dioxins in chlorinated UK water supplies.

To assess the generation of by-products and mutagens by water treatment disinfectants.

To review developments likely to affect future legislation on disinfection by-products and implications for the UK, especially of the revised WHO guidelines for drinking water, and carry out appropriate investigations.

To review and develop models covering disinfection by-product formation and chemical/microbial risks.
3. PROGRAMME COVERED

The programme element covered by this report is as follows:

The developments in the United States Environmental Protection Agency (USEPA) on i) modelling DBP formation in water treatment and ii) microbial risks etc., will be critically reviewed and attempts at deriving models for the UK will begin. The latter will use existing information on, e.g. incidence of pathogens in water sources, removal by treatment, resistance to disinfection, infective dose and impact on consumers.

Successive sections of this report will examine:

1. Microbial disease - its features, surveillance and epidemiology, assessment of infectivity and basis for legislation.

2. Chemical toxicity - its features, DBPs, assessment of risks and basis for legislation.

3. The disinfection process - its role as part of the multiple barrier concept, disinfectants and disinfection kinetics, basis for legislation.

4. The USEPAs regulatory strategies - the surface water treatment rule, derivation and use of CT values, risk assessment modelling for infectivity and DBP formation, results of modelling.

5. Appraisal of alternative strategies for balancing chemical and microbial risks.

6. Recommendations for development of models and concepts for DBP formation and for overall risk assessment.
4. MICROBIAL DISEASE

4.1 Features

Infectious diseases caused by pathogenic bacteria, viruses and protozoa or by parasitic animal life are the most common and widespread health risk associated with drinking-water. Excluding trachoma, world-wide statistics provided by WHO show 1.2 billion cases of water-related illnesses and 5 million deaths yearly for developing countries (Helmer 1991). The success of providing properly treated water supplies is shown, in contrast, by the figures for the UK, which indicate an average of 200 cases yearly for public water supplies and no deaths over the past 50 years, excluding the epidemic of typhoid fever at Croydon in 1937 (Galbraith et al. 1987). Over this period, 1937-86, of the 11 outbreaks involving public supplies, including Croydon, eight were associated with no chlorination or defective chlorination and of 13 outbreaks involving private supplies, all were associated with defective chlorination or no chlorination at all.

The following features of waterborne microbial diseases distinguish them from chemically induced illnesses and toxicoses:

- They are acute
- Outbreaks erupt suddenly
- Pathogens multiply in the host and are excreted
- Secondary infections occur
- Carriers may remain in the community, as reservoirs of infection
- Pathogens decay in the environment
- Outbreaks evoke great public response
- All ages are infected, particularly the young
- Infection often confers lasting immunity

These features have a number of implications for operation of water treatment plants and for policies to control disease. The suddenness with which outbreaks occur and the public’s response demands immediate action to detect the cause and render the supply safe. There will be considerable disruption to household activities, to industries relying on pure and wholesome supplies and to hospitals and medical care if emergency supplies have to be introduced and public confidence in water supplies will be lost.

Environmental decay and removal of pathogens by water treatment processes provides the basis for providing multiple barriers to the transmission of infection. Because perpetuation of water borne disease requires successful environmental transmission through sewage and drinking water to new hosts, the condition for preventing disease is that there should be a net loss of pathogens around the cycle of infection. People who recover but continue to carry infection and excrete pathogens, often sporadically, are a well known hazard. If infection confers lasting immunity, a skewed age distribution of immunity will be induced
in the community, in which the youngest are most at risk. In communities where waterborne infectious diseases are endemic, this has serious repercussions for economic growth and productivity, since it is those of working age, or approaching it, who are most affected.

4.2 Infection and immunity

Immunity, conferred as a response to challenge by pathogens and production of antibodies in the blood is one of the mechanisms by which man counters infections. The body also possesses other, more general or non-specific forms of immunity, such as those provided by the integrity of the skin, the antibiotic properties of the tears and mucous secretions, the digestive juices and scavenging activities of the phagocytic white cells in the blood. Infection may also be determined by specificity of the pathogen for particular hosts and by the age or state of health of the individual. Environmental factors, such as housing, safe water supplies and mains drainage are potent factors in immunity of the community.

These reasons collectively determine the difficulty of assigning an infectious dose for a given pathogen in man. To this, must be added differences in the invasiveness of the pathogen and its ability to produce toxins. For example, there will be differences in infectivity between strains of the same species. The infectivity of a strain taken directly from an acute case of disease will be high, but this will diminish with exposure to the natural environment.

4.3 Surveillance and epidemiology

Surveillance has been defined by the World Health Organization (WHO 1976) as the continuous and vigilant public health assessment and overview of the safety and acceptability of drinking-water supplies. In the wider field of communicable disease, it provides an early warning of emerging diseases and outbreaks, caused by changing circumstances or recognised by improvements in isolation methods and diagnosis, and of the need to take investigative and corrective action.

Two surveillance procedures exist in Great Britain for waterborne disease.

Statutory notifiable diseases, diagnosed on the medical opinion of the doctor, include cholera, typhoid and paratyphoid fevers, bacillary and amoebic dysentery and viral hepatitis. These are reported by the patient’s doctor to the local Medical Officer for Environmental Health (now usually the Consultant in Communicable Disease Control) and thence to the Office of Population Censuses and Surveys (OPCS) for publication in the Registrar General’s Weekly Return (McCormick 1993).

In England and Wales, the Public Health Laboratory Service’s Communicable Disease Surveillance Centre (PHLS-CDSC) and, in Scotland, the Communicable Diseases (Scotland) Unit (CDSU) record the results of the examination of clinical specimens,
referred to Public Health Laboratories by general practitioners and hospitals and can be called to investigate suspected outbreaks of disease by the proper medical advisors of local authorities.

Under the provisions of *The Water Supply (Water Quality) Regulations* (Statutory Instrument 1989) water companies are required to designate water supply zones (Section 2). Water undertakers are also required (Section 30(S)) "...to notify a local authority and a district health authority as soon as may be after the occurrence of any event which, by reason of its effect or likely effect on the water supplied by it, gives rise or is likely to give rise to a significant risk to the health of persons residing in the authority’s areas." If the event involves the detection of a potential pathogen or evidence that a potential pathogen could be present the district health authority will form an Outbreak Control Team (OCT) to investigate any illness which occurs in the community. The Consultant in Communicable Disease Control and the CDSC would be involved in the OCT. Such action will facilitate testing the hypothesis that an outbreak might be related to drinking water.

Both the CDSC and the CDSU release weekly reports on notifications with summaries of the results of the more significant investigations. Additionally, from 1991, the CDSC has commenced a pilot reporting scheme for waterborne disease, by which Public Health Laboratories submit weekly questionnaire forms detailing information upon cases involving the following classes of incident.

- Suspected water consumption
- Water contamination
- Recreational water exposure
- Travel association
- Comments and other information.

Quarterly summaries of results are sent to participating laboratories. A similar pilot reporting scheme has been initiated by the CDSU.

Epidemiology is the study of the means by which diseases are spread. In the case of an outbreak of disease occurring, teams will be despatched to the site of the outbreak with the aim of determining the likely causes. The methods used were reviewed in a workshop held by the USEPA (Craun 1990a). The rate and degree of spread of infectious disease can also be modelled, for example, using communities of mice or other laboratory animals, infected under controlled conditions or by computer simulations in hypothetical communities of healthy, infected or immune individuals, distributed in simulated time and space.

It is seldom possible to obtain any indication of the infecting dose which caused a waterborne outbreak. This is because the pathogen will have decayed or have been flushed through the distribution system before the outbreak is detected and the water is
analysed. The finding of the pathogen in supply and in infected subjects provides strong proof for water as the vehicle. However, attack rates seldom exceed a few per cent of the population served by the supply. This indicates that a small percentage of the population are unduly sensitive and/or that numbers of pathogens encountered are very low.

4.4 Infectivity studies with volunteers

Much of the information upon infectious doses has been obtained in experiments with human volunteers (who are fed non-virulent strains or whose infections are aborted by antibiotic therapy) or with experimental animals. In these experiments, groups of volunteers are given stratified doses and infection is determined by symptoms of the disease or excretion of the pathogen in numbers indicating multiplication in the body. Generally, it is found that there is an approximately linear relation between the logarithm of the dose (number administered) and the percentage of subjects falling ill, transformed to the probit scale (i.e. the percentage points of the standard normal distribution). This linearisation (probit analysis) enables the median infective dose, ID$_{50}$, to be estimated (Figure 4.1). However, because the numbers of experimental subjects is necessarily small, the estimates of the ID$_{50}$ are imprecise and little meaning can be given to extrapolations for low doses, which are those of most concern for contamination of drinking water supplies.

These points are shown in Figure 4.1, which re-analyses data for the enteric pathogens Shigella spp. (Figure 1a; Dupont et al. 1989), for rotavirus (Ward et al. 1986) and for the enterovirus Echovirus 12 (Shiff et al. 1984). The total numbers of subjects in each study (30-283) would be difficult to recruit, yet the imprecision is obvious. In Figure 4.1 all the experimental data points for dose/response are plotted. Where all or none of the volunteers were infected, the points cannot be included in the probit analysis. The slopes of the regression lines show that there is an enormous difference in the sensitivity of individuals to infection.

Because of the interest in viruses as agents of waterborne disease, in outbreaks where no bacterial pathogen could be isolated there has been much speculation upon the ‘minimal infective dose’ of viruses to man. This dates from a symposium on ‘Transmission of Viruses by the Water Route’ (Berg 1966) sponsored by the US Federal Water Pollution Control Administration in 1965. A paper on the ‘Minimal Infective Dose’ by Plotkin and Katz (1966) reviewed experimental evidence for median infective doses for man by the oral, respiratory and ophthalmic routes and deduced that one infective dose for tissue culture cells (plaque-forming units, PFU, or titre infecting 50 per cent of tissue cultures, TCD$_{50}$) was sufficient to infect man, “if it is placed in contact with susceptible cells”. The words quoted are important, if only to emphasise that the oral infectivity studies were of poliovirus vaccine strains, which are highly infective, and that one study by the authors was with premature infants fed in the first three days of life. Subsequent research with experimental infections does not support the view that the median infective dose, ID$_{50}$, for waterborne viruses amounts to about one infective unit for tissue culture cells (c.f. Figure 4.1b) although the values are often small. The wide variability in susceptibility of individuals does suggest that a small number of people in the population could acquire infection from average doses of one infective unit or less.
Figure 4.1 Relationships between doses of (a) *Shigella* spp. (Dupont et al. 1989) and (b) Echovirus 12 (Schiff et al. 1984) and rotavirus (Ward et al. 1986) and percentages of human volunteers infected. Arrows indicate calculated ID$_{50}$, numbers of subjects in each trial shown in percentages.
Virologists have long suspected low-level transmission of enteric viral infections by water (Rao and Melnick 1986). This is difficult or impossible to demonstrate by epidemiology, because of the broad spectrum of symptoms, which are not necessarily gastro-intestinal, and because low doses may give rise to asymptomatic excretion. In such cases, large numbers of viruses will nevertheless be passed in faeces and enter the water cycle, perhaps perpetuating the infection of the community.

4.5 Mathematical models of infection

An insight may be gained into the mechanisms of infection by constructing models of the process as hypotheses and testing the predictions against experimental data. The modelling of epidemic spread of disease in the community is a further stage, which will not be considered here, although it is the subject of a reference monograph on the mathematical theory of epidemics (Bailey 1975).

Two approaches are used in modelling infection, deterministic and stochastic. In the first, the pathogens in the dose are considered to act co-operatively. Illness or death results from their joint action. In the second, the pathogens are assumed to act independently, so that more than one are needed to cause infection or death, because the probability of a single pathogen doing so is less than one. The situation has been likened by Meynell and Stocker (1957) to a poor marksman firing at a bottle, who given long enough, may eventually shatter the bottle. A distant observer might conclude that the build-up of stress might have caused the bottle to break eventually, but one on the spot may note that a single chance shot hit the bottle.

Haas (1983) analysed these two different approaches for their success in modelling risks from low doses of pathogens. He identified three models, one deterministic, the other two related and stochastic.

4.5.1 Log-normal deterministic model

Under this hypothesis, each subject is assumed to have an inherent minimal infective dose and if exposed to a dose in excess, then infection (or disease) will result. If the entire study population is exposed, each to a dose of N pathogens and the minimum infective doses for the population are distributed log-normally, with a log mean of μ and log standard deviation of σ, the probability P, of an individual becoming infected (or ill) is described by

\[ P = \frac{1}{(2\pi)^{0.5}} \int_{-\infty}^{\infty} \exp\left(\frac{-Z^2}{2}\right) dZ \]  

(1)

where the standard normal deviate \( Z = (N - \mu)/\sigma \) 

(2)

These relationships are the basis of probit analysis (Section 4.4 and Figure 4.1), in which \( \mu \) is equivalent to the median infective dose ID\(_{50}\) and \( \sigma \) is represented by the slope of the regression line.
A little thought will show that the co-operative conditions of this model are likely to apply to chemical poisoning and cumulative toxicity, but may not model infection by a highly infective and virulent pathogen.

4.5.2 Single-hit exponential model

This stochastic model assumes that only one pathogen need survive until it can arrive at the target site in the body and infect. Furthermore, the pathogens are randomly distributed in the water. If the average dose is \( N \) pathogens, which each have a constant probability, \( r \), of surviving to infect, the probability of infection is

\[
P = 1 - \exp(-rN) \tag{3}
\]

Haas notes that, although this model may fit some \textit{in vitro} or most probable number assays of infection, the slopes of the plot of \( P \) on \( \log N \) are less steep than predicted by this equation. One explanation is variation in the virulence of individual pathogens and/or the sensitivity of individual hosts, i.e. \( r \) is not constant.

4.5.3 The beta-distributed model

Haas (1983) has attempted to correct for deviation from Equation 3 by supposing that \( r \), the probability of a pathogen surviving to infect is not constant, but distributed as a range of values, described by the empirical terms \( \beta \) and \( \alpha \) which represent the mean and standard deviation respectively of the survival to infect in Equation 4:

\[
P = 1 - \left(1 + N/\beta \right)^{-\alpha} \tag{4}
\]

4.5.4 Comparison of the three models

Haas (1983) compared the ability of the three models to fit his own or others’ published data from infectivity trials with stratified doses of the pathogens listed in Table 4.1. The single-hit model of Equation 3 failed to fit five of the nine sets of data. All three models provided similar estimates of the median infective dose. At low doses, the log-normal model deviated from the predictions of the two stochastic models by predicting much lower risks. He concluded that the stochastic type of model provided a conservative estimate of risk with low doses and that it was impossible to rule out the hypothesis that one organism, when ingested could cause disease in at least a proportion of the exposed population.
4.5.5 Prediction of risk and its precision

Table 4.1 suggests strongly that extrapolation of infectivity data to estimate risks from low doses of pathogens provides widely divergent estimates. The data and estimates of Table 4.1 and of similar infectivity studies relate to single, point doses, whereas in drinking water supply over long periods and ultimately over a lifetime, a person would be exposed to many challenges. If the individual exposures to pathogens are statistically independent and no long-lasting or temporary immunity is induced, the ultimate risk over a long period is a multiplicative function (not a summation) of the risks from point exposures. The errors in estimation of the point exposure risk are similarly multiplied.

Haas et al. (1993) examined the rotavirus/human infectivity data of Ward et al. (1986; Figure 4.1), to explore its applicability for assessing viral risks in drinking water and thereby examined the degree of variability in prediction. It is instructive to examine the stages which they used in assessing risk.

Using the beta-distributed model, Equation 4, maximum likelihood analysis (a similar approach to that used for deriving most-probable numbers in bacterial dilution counts) derived an ID$_{50}$ of 5.6 rotavirus particles (c.f. the value of 6.0 in Figure 4.1 by probit analysis) and a value of $\alpha = 0.265$, showing that the dose-response was shallower than exponential (Equation 3). The confidence limits of the ID$_{50}$ were not given.

It was then noted that Payment et al. (1985) had found an average count of 0.0006 enterovirus pfu/l in Montreal drinking water. Twice this value, 0.0012/l, was used to estimate the most exposed individual and daily consumption was taken as 1.7 l/head. The point risk estimate of daily probability of disease, $P_d$, was estimated from the beta-distributed model as 0.000717. The annual risk, $P_y$, assuming equivalent and independent daily challenges was calculated from

$$P_y = 1 - (1 - P_d)^{365}$$

as 0.23. These values compared with an annual risk of gastro-enteritis disease in Montreal of 0.24 cases/person-year (Payment et al. 1985) and a calculated value (Equation 5) of the observed daily risk of 0.00082. The near coincidence of observed risks and predicted would be remarkably close but for the facts that the estimated risks were derived from infectivity of man by rotaviruses and average numbers of enteroviruses in Montreal water over different periods of time from the epidemiological studies of gastro-enteritis. Furthermore, the 95 per cent confidence limits of the calculated daily risk are extremely wide (Haas 1993), $2 \times 10^{-5}$ to 0.2.
Table 4.1  Comparison of the three infectivity models in deriving median infective dose, ID<sub>50</sub>, and extrapolated risk of infection from ingesting a mean dose of 10<sup>3</sup> pathogens (Haas 1983)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Log-normal</th>
<th>Single-hit</th>
<th>Beta-distributed</th>
<th>Log-normal</th>
<th>Single-hit</th>
<th>Beta-distributed</th>
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<td><em>Salmonella typhi</em></td>
<td>DR</td>
<td>DR</td>
<td>DR</td>
<td>3.3 x 10&lt;sup&gt;9&lt;/sup&gt;</td>
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<tr>
<td><em>Shigella dysenteriae</em></td>
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<td>DR</td>
<td>500</td>
<td>3.3 x 10&lt;sup&gt;9&lt;/sup&gt;</td>
<td></td>
<td>5 x 10&lt;sup&gt;6&lt;/sup&gt;</td>
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<tr>
<td><em>Shigella flexneri</em></td>
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<td>DR</td>
<td>DR</td>
<td>3.3 x 10&lt;sup&gt;9&lt;/sup&gt;</td>
<td></td>
<td>1.5 x 10&lt;sup&gt;6&lt;/sup&gt;</td>
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<tr>
<td><em>Shigella flexneri</em></td>
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<td>64 000</td>
<td>4.2 x 10&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
<td>1.3 x 10&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Entamoeba coli</em></td>
<td>14</td>
<td>DR</td>
<td>77</td>
<td>3.0 x 10&lt;sup&gt;9&lt;/sup&gt;</td>
<td>1.2 x 10&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1.7 x 10&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Echovirus 12</td>
<td>55</td>
<td>58</td>
<td>53</td>
<td>ca 10&lt;sup&gt;9&lt;/sup&gt;</td>
<td>1.2 x 10&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1.5 x 10&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Poliovirus 1</td>
<td>60</td>
<td>57</td>
<td>47</td>
<td>3.0 x 10&lt;sup&gt;9&lt;/sup&gt;</td>
<td>2.6 x 10&lt;sup&gt;4&lt;/sup&gt;</td>
<td>6 x 10&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Poliovirus 1</td>
<td>DR</td>
<td>DR</td>
<td>67 500</td>
<td>2.3 x 10&lt;sup&gt;7&lt;/sup&gt;</td>
<td>2.6 x 10&lt;sup&gt;4&lt;/sup&gt;</td>
<td>4.4 x 10&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Notes:  DR = distribution rejected with probability exceeding 0.95.

Data are for adult volunteers displaying infection, except *S. dysenteriae* for disease. The original data (his Table 3) also provided estimates of risk for doses of 10<sup>4</sup> and 10<sup>5</sup> pathogens.
Haas (1993) noted that the most infectious organism, for which human infectivity data exists, is Poliovirus III, with an ID₅₀ of 3.4 pfu and α = 0.500. Using the calculations given above (Equation 5), the annual risk of illness from poliomyelitis with the Montreal observations was calculated as 0.175, or 17.5 per cent, a level which is clearly untenable. This is because detection of enteroviruses in water does not equate to detection of viruses capable of causing overt disease. Such calculations also make no allowances for development of immunity in people who have been exposed to the pathogens. Furthermore, ‘infection’ in experimental studies is defined as excretion of pathogens (which have multiplied in the body), or development of antibodies, and not the appearance of the symptoms of clinical illness, for which, much larger doses are needed.

This detailed description of the methods of modelling has been given because they have been used in support of US policies for treatment and disinfection of drinking water to control *Giardia* (Clark 1990, Clark and Regli 1991, Rose *et al.* 1991) and other pathogens (Haas 1993). This aspect will be described in Section 7, when the USEPA’s policies for balancing microbiological and chemical risks are described.

### 4.6 Basis for legislation and control

It is axiomatic that drinking water must not contain pathogenic organisms. Because the isolation of pathogens is at least tedious, if not impossible, regulatory and operational microbiological examination, for the last 110 years has concentrated on demonstrating the absence of bacteria indicative of faecal contamination (Report 1995). The rationale of the microbiological indicators is that they greatly outnumber any enteric pathogens and decay at rates similar to enteric pathogens, or less rapidly, giving considerable margins of safety. At the same time, the philosophy of protecting treated waters against pollution in distribution and of treating surface waters by filtration dates at least from the Metropolis Water Act 1852 (Scratchley 1888), as a direct reaction to epidemics of cholera in London in the first half of the nineteenth century. This has progressively evolved into the requirement for maintaining multiple barriers to the spread of infection (Ministry of Health 1948), the recommendation for disinfection of treated water entering supply and maintaining residual disinfectant in supply (Water Authorities Association 1988) and, in Statutory Instrument (1989), the definition of ‘wholesomeness’ of drinking water (Section 3) and the requirement for water to be disinfected (Section 22).

*The Regulations* (Statutory Instrument 1989) define “wholesomeness”, *inter alia*, by reference to numerical standards for the common faecal indicator bacteria, consistent with the standards in the drinking water Directive. They include a ‘catch-all’ requirement that a water will be wholesome, provided it does not contain any other (other than a parameter) element, organism or substances at a concentration or value detrimental to health.

The philosophies of absence of faecal indicator bacteria, treatment of surface waters, creation of multiple barriers to transmission of infection and protection of water in distribution from contamination are re-endorsed in the World Health Organization’s, *Guidelines for Drinking-Water Quality* (WHO 1993). Terminal disinfection is regarded as
the last step in the chain of treatment and WHO recognises that the conditions for efficient disinfection are met best by a water which is already of high quality and has received appropriate treatment. These principles are justified by many years experience.

Similar principles have evolved in North America since the beginning of the Century, but with a greater degree of enforcement by Federal and State legislature. The test for coliform bacteria assumed legal status in some states, notably California, from the early 1940's, prompted by a study which confirmed similarity of decay rates of coliform bacteria and bacterial enteric pathogens, the constancy of the coliform to pathogen ratio during sewage treatment and natural self-purification and a deduction that a single typhoid bacillus could account for the disease in a small fraction, possibly 1-2 per cent of the community drinking such water (Kehr and Butterfield 1943).

In recent years, giardiasis has emerged as the major identifiable cause of waterborne disease in the US (Table 4.2). This, coupled with several major epidemics of cryptosporidiosis and the recognition that enteroviruses might be detected with large-volume monitoring in water otherwise of satisfactory bacteriological quality (Payment et al. 1985) support current US Federal Legislation under the Safe Drinking Water Act. This requires the US Environmental Protection Agency to publish National Primary Drinking Water Regulations, setting either a maximum contaminant level (MCL) or a water treatment technique requirement for contaminants which may have an adverse effect on health (Berger and Regli 1990). They include a requirement for total coliform bacteria to be absent from 100 ml samples in at least 95 per cent of samplings (Coliform Rule) and for surface waters and waters under their influence to receive filtration (unless meeting specific conditions of catchment control and purity) and to be disinfected (Surface Water Treatment Rule, STWA; USEPA 1989a). The SWTR is an essential difference between US and UK practice, since it specifies treatment performance, rather than quality of the finished water.

The SWTR specifies that the treatment and disinfection process must together guarantee 99.9 per cent removal or inactivation of cysts of *Giardia lamblia* and 99.99 per cent removal or inactivation of viruses. This mandates water treatment to yield not more than one case of giardiasis annually per 10^4 consumers (i.e. a risk of 10^-4) as a goal. This is against a background of giardiasis which, at the time of development of the SWTR, was the most significant identifiable waterborne infection in the US associated with inadequately treated surface water supplies and against annual risks of waterborne infectious disease and of mortality in the US of about 4 x 10^-6 respectively (Regli et al. 1993a). Conformity with the SWTR is decided, not by monitoring for *Giardia* cysts, but by recording the concentration, C, of disinfectant leaving the plant and the time taken, t₁₀, for the concentration of a step-injected tracer to reach 10 per cent of its ultimate concentration (or 10 per cent of its injected concentration) in the effluent. The product, C x t₁₀, is referred to standard tables in a *Guidance Manual* (USEPA 1989b), to ascertain if the disinfection stage of the treatment plant is in compliance. The theoretical basis for the C.t concept is described later in Section 5.4.
Table 4.2  Aetiology of water borne disease in the US, 1971-1985 (Craun 1990b)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage of outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undefined acute gastro-enteritis</td>
<td>50</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>18</td>
</tr>
<tr>
<td>Chemical poisoning</td>
<td>10</td>
</tr>
<tr>
<td>Shigellosis</td>
<td>7</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>5</td>
</tr>
<tr>
<td>Viral acute gastro-enteritis</td>
<td>4</td>
</tr>
<tr>
<td>Campylobacterosis</td>
<td>2</td>
</tr>
<tr>
<td>All others</td>
<td>4</td>
</tr>
</tbody>
</table>

The SWTR was developed just before the significance of Cryptosporidium spp. as agents of waterborne disease were recognised in the US, particularly in the case of plants treating surface water and where filtration was defective. The oocysts are unaffected by chlorination and are partly resistant to disinfection by chlorine dioxide, ozone and ultraviolet radiation. The decision was taken in 1989 to finalise the STWR using Giardia and viruses as target pathogens and to include Cryptosporidium when more data were available. Discussion (Pontius 1993a) on the proposed Disinfectants - Disinfection By-Products Rule by an advisory committee, raised the question of whether or not the SWTR adequately protects against cryptosporidiosis. This committee has proposed, (a) an Information Collection Rule, to provide necessary data and (b) and interim Enhanced Surface Water Treatment Rule (ESWTR, effective 1997-1998) and a final ESWTR (1998-2000) (Pontius 1993b).

4.7  Cancer and infectious diseases

It is now becoming realised that certain infections, by causing chronic cellular damage, can predispose to cancer.

Hepatitis B and C viruses have been evaluated by the International Agency for Research on Cancer (IARC 1994a) of WHO, who conclude that chronic infection is carcinogenic to humans (Group 1). Infection with Hepatitis D virus is not classifiable as to its carcinogenicity to humans. None of these viruses is transmitted by water and the faecal-oral route. All three can run a chronic course, unlike the infections with Hepatitis A and Hepatitis E viruses, which are known to be waterborne. IARC (1994a) note that, “The few studies which have been done found no association between infection with hepatitis A virus and hepatocellular carcinoma and no studies of hepatitis E virus have been reported in this connection.”
Infections with schistosomes (blood flukes) and liver flukes have shown relationships with cancer in humans (IARC 1994b). However, these infections, although waterborne or water-associated, are not endemic in Western Europe.

The bacterium, *Helicobacter pylori*, has recently been recognised as a major agent of gastritis and of gastric and duodenal ulcers. It specifically infects the gastric mucosa and is present in about 70% of patients with gastric ulcers. The symptomless carriage rate is high and increases with age. In a French study reported by IARC (1989a, b, p184), seropositivity rose from less than 5% in 0-9 year olds, rising to over 30% in those older than 40 years. The modes of transmission are a matter of speculation and the most likely route appears to be person-to-person. However, there is some circumstantial evidence for involving the water route. since *H. pylori* is eliminated with faeces and IARC note (p186) that vegetable fertilised with sewage were a risk factor in Chile, consumption of municipal water was a risk factor in children in Lima, Peru and that *H. pylori* was detected by the polymerase chain reaction in sewage in Peru. IARC conclude that there is sufficient evidence in humans for the carcinogenicity of infection with *H. pylori* (Group 1).

This section indicates that proper treatment of water and terminal disinfection must be considered as having a positive role, at least in developing countries, in reducing cancer risks, by controlling those parasitic infections. If the water route is significant in the spread of *H. pylori* infection, the same conclusion may be drawn.
5. TREATMENT AND DISINFECTION

5.1 Water treatment

The aim of water treatment is to produce water which is wholesome and not injurious to health. World-wide guidance is given by the World Health Organization's (WHO 1993) Guidelines for Drinking-Water Quality. These specifically recognise that:

“Infectious diseases caused by pathogenic bacteria, viruses and protozoa or by parasites are the most common and widespread health risk associated with drinking water” (p8).

“Disinfection is the final safeguard and also protects the water during distribution against external contamination and regrowth. The whole treatment sequence may indeed be regarded as conditioning the water for effective and reliable disinfection” (p133).

“Terminal disinfection of piped drinking-water supplies is of paramount importance and is almost universal, as it is the final barrier to the transmission of waterborne bacterial and viral diseases” (p135).

The extent of treatment depends upon the quality of the source water. Groundwaters are usually of consistently high quality and require minimal treatment. Surface waters, especially lowland rivers, are generally of a lower quality and require more extensive treatment.

5.2 Guidance and legislation

Strategies for supplying safe water depend upon careful selection of source, the selection of appropriate treatment, final disinfection and protection of the finished water by piped distribution until it reaches the consumer. All these strategies create multiple barriers to the transmission of infection. They are the basis for the advice given by WHO (1993) for ensuring microbiological safety of drinking water.

In the UK, the importance of multiple barriers and for the control and recording of chlorination were recognised after the outbreak of typhoid fever in Croydon in 1937 (Ministry of Health 1938), by the immediate issue of official guidance on the administration of water undertakings. This advice has been updated over the years to meet evolving needs and is now represented by the Operational Guidelines for the Protection of Drinking Water Supplies (WAA 1988). Disinfection is now a requirement under Section 23 (1) of the Water Supply (Water Quality) Regulations (Statutory Instrument 1989), which implement the microbiological and chemical requirements of the drinking water Directive 80/778/EEC.
US legislation for the microbiological quality of water has been summarised in Section 4.6. The Surface Water Treatment Rule (SWTR) (USEPA 1989a) defines performance levels - 99.9% (i.e. 3 log₁₀ units) removal or inactivation of Giardia cysts and 99.99% (4 log units) of viruses, based on design and operating conditions for filtration and disinfection together. Well-operated plants, which achieve design, operational and turbidity performance criteria are assumed to achieve 2-2.5 log units removal of Giardia cysts and 1-2 log units removal of viruses by filtration alone. The theoretical degree of inactivation by disinfection is determined by measuring the product of disinfection concentration, C (mg l⁻¹) and contact time, t (min) and referring the ‘C.t value’ to tables in a guidance manual (USEPA 1989b). The SWTR also requires at least 0.2 mg l⁻¹ of the disinfectant to be maintained in the water entering the distribution system and a detectable residual at all times in the system itself. The rationale for the C.t concept is explained in Section 5.4.

5.3 Disinfecting agents

Chlorine (liquid chlorine or hypochlorite) is the commonest disinfectant, although chloramines, chlorine dioxide, ozone and ultraviolet radiation are used. The chemical agents may be dosed at other stages during treatment, as pre-oxidants, to improve performance of coagulation, remove iron and manganese, reduce biofouling and render recalcitrant organic carbon more biodegradable. Ultraviolet radiation is used as a terminal disinfectant and may also be used with ozone for achieving oxidation of pesticides and other organics.

Much of the information in this section was taken from the Water Treatment Handbook (Hall and Hyde 1992) and the monograph by White (1992).

5.3.1 Chlorine

Chlorination of treated water is the most commonly used practice of disinfecting supplies before distribution. The simplest approach is to use marginal chlorination where a minimum dose of chlorine is added to achieve the desired free chlorine residual concentration after a given contact time. However, marginal chlorination is only effective if ammonia and other reacting substances are absent or at very low concentrations. When ammonium compounds are present, breakpoint chlorination is normally used, in which sufficient chlorine is added to exceed the chlorine demand for chloramine production and ensure the presence of a free chlorine residual. Usually dechlorination is necessary, using sulphur dioxide, to reduce the high chlorine residual to an acceptable concentration before distribution.

The effectiveness of chlorination depends on maintaining the desired concentration for a minimum period and is influenced by the quality of the water and its pH. Chlorine in solution is instantaneously hydrolysed to an equilibrium mixture of hypochlorous acid and hypochlorite ion. The former is approximately 100 times more active in killing Escherichia coli than the latter. The equilibrium is strongly pH-dependent. The percentages of hypochlorous acid by weight at 20 °C in water at pH 5, 7 and 10 are
respectively 99.8%, 27% and 0.38%. After dosing, chlorine concentrations decrease with time, usually over several hours, because of reaction with other compounds in the water. This reduction over a given time period is termed the chlorine demand. Surface waters generally have a higher chlorine demand than groundwater and higher doses are required to achieve the desired residual concentration.

WHO (1993) recommend for disinfection a minimum free chlorine concentration of 0.5 \( \text{mg} \, \text{l}^{-1} \) after a contact time of 30 minutes at a pH below 8, provided that the turbidity does not exceed 1 NTU. Such disinfection, in combination with appropriate treatment, is recommended to produce water with negligible viral risk. The control of parasites and other invertebrate life in water mains is best accomplished by proper operation and control of water treatment processes and distribution practices. In particular, the use of measures to reduce viruses, together with attainment of the microbiological guidelines, should, except in extraordinary cases of extreme contamination, ensure that the water has a negligible risk of transmitting parasitic diseases.

The reaction of chlorine with organic and inorganic substances in water will result in formation of by-products by chlorination or oxidation, some of which are known to produce taste and odour, to be toxic or carcinogenic. Those which are known to be carcinogenic or otherwise of concern to health are listed in Section 6.1.

### 5.3.2 Monochloramine

The formation of chloramine is sometimes desirable as it possesses a more stable residual than chlorine and can therefore persist longer in distribution systems. Chlorine produces monochloramine and dichloramine by reaction with ammonia, which is either naturally present in the water or after dosing with ammonium sulphate. The chlorine dose must be controlled to prevent the formation of nitrogen trichloride or high concentrations of dichloramine which can lead to taste and odour complaints. Incorrect dosing can produce nitrite from bacterial metabolism of excess ammonia. Monochloramine is approximately 500 times less active as a disinfectant of \textit{E. coli} than hypochlorous acid and dichloramine even less so.

As chloramines are less active oxidising and chlorinating agents than free chlorine, they are less likely to produce toxic by-products.

### 5.3.3 Chlorine dioxide

Chlorine dioxide is formed in the reactor by oxidising sodium chlorite with chlorine or sodium hypochlorite, or by reaction of chlorite and hydrochloric acid. Chlorine dioxide forms fewer trihalomethanes and other chlorinated by-products than chlorine provided excess chlorine is not present. It can, however, increase the concentrations of chlorite and chlorate in treated water which limits its suitability as a disinfectant. A less stable residual is formed by chlorine dioxide compared to chlorine and may require the addition of chlorine to maintain a disinfectant residual in distribution.
The efficiency of chlorine dioxide as a disinfectant is similar to that of free chlorine for most micro-organisms but appears to be more effective against *Giardia* cysts and *Cryptosporidium* oocysts. White (1992, p1018) provides evidence that chlorine dioxide was superior to combined chlorine in disinfecting poliovirus I in secondary wastewater effluent. Chlorine dioxide is more effective as the pH increases over the range 6 to 9 but above pH 10 it disproportionates to chlorite and chlorate, which have no biocidal activity.

### 5.3.4 Ozone

Ozonation depends upon the application of a sufficient dose to achieve the desired concentration after a given contact time. The required dose is influenced by water quality. Ozone is a more powerful oxidising agent than chlorine and so reduced concentrations and contact times are required for disinfection. A typical dosing regime would be 0.4 mg l\(^{-1}\) residual after a maximum contact of 4 minutes (Hall and Hyde 1992). Ozone is, to some extent, effective against *Giardia* cysts and *Cryptosporidium* oocysts. However, after ozonation there is no persistent residual to maintain biocidal activity during distribution.

Fewer disinfection by-products are formed by ozonation and these are principally organic oxidation products. The identified by-products of health concern are bromate and bromoform (Trussell 1993). However, ozone converts some of the recalcitrant organic carbon into compounds which can be readily utilised by micro-organisms. These include glyoxal, methyl glyoxal, aldehydes and fatty acids. Increased concentrations of assimilable organic carbon may promote microbial proliferation during distribution and cause a deterioration in water quality. This oxidative property is now being increasingly exploited by combining ozonation and granular activated carbon filtration (as a biological filtration stage) to remove assimilable organic carbon before terminal disinfection and to obtain a biologically stable water.

### 5.3.5 Ultraviolet radiation

Ultraviolet radiation (UV) is used for disinfection of water supplies either as an alternative to, or a partial replacement for chemical oxidants. Maximum biocidal efficacy is achieved by irradiation at wavelengths of around 260 nm, at which the absorbance of microbial deoxyribonucleic acid (DNA) is maximal. The energy radiated by the low-pressure mercury vapour discharge tube is mainly in the line of wavelength 253.7 nm. The lethal effect is by creating thymine dimers in the DNA, which, if irreparable, cause deleterious gene mutations and cell death. Its efficacy is influenced by water quality as soluble organic carbon strongly absorbs UV and because bacteria attached to particles may be shielded from the radiation. The reactors have the advantage of being compact, as the water is passed through the UV-transparent irradiation column and no storage or dosing is required for chemicals. However, there is no residual to maintain biocidal activity during distribution and efficiency progressively falls off as the walls of the irradiation column become fouled and the UV lamp ages.
It has been claimed that intense ultraviolet radiation causes photolysis of organic micropollutants, thereby releasing assimilable organic carbon and enhancing microbial spoilage and biofilm growth in distribution. Current research is investigating a combination of UV and ozone to remove potentially harmful chemical pollutants.

An ultraviolet dose of about 15 mWs cm\(^{-2}\) should be sufficient to give 99.9 percent inactivation of most micro-organisms (data from Hall and Hyde 1992), using radiation mainly at 253.7 nm. It was suggested that units should provide a minimum dose equivalent to 25 mWs cm\(^{-2}\) at a wavelength of 253.7 nm to give a margin of safety.

Ultraviolet radiation is effective against most bacteria and viruses. However, it is much less effective against Giardia cysts and Cryptosporidium oocysts and the doses required for 99.9% inactivation cannot be practically achieved in water treatment.

5.4 Kinetics

5.4.1 Theory

Early studies on the kinetics of disinfection were undertaken by Chick (1908) and lead to the relationship that the fraction of the original population surviving disinfection after a given time period is constant. Chick's Law is expressed mathematically as:

\[
\log_{10} \frac{N}{N_0} = -kt
\]

(6)

where \(N\) is the number of micro-organisms after the time interval \(t\), \(N_0\) the initial number of micro-organisms and \(-k\), the specific death rate constant.

The rate constant, \(-k\), varies as a function of the species of micro-organisms and the type of disinfectant and its concentration. The validity of this relationship depends upon certain assumptions about the nature of the disinfection process. It is assumed that all cells are equally susceptible to disinfection and are not protected from its biocidal activity through clumping or extracellular polymeric material.

This model (Equation 6) was refined by Watson (1908), using the same data as Chick, to produce an empirical relationship that incorporates changes in the concentration, \(C\), of disinfectant. This relationship is referred to as Watson's empirical dilution law or more usually, Watson's Law and is represented mathematically as:

\[
\log_{10} \frac{N}{N_0} = -AC^n t
\]

(7)

where \(-A\) is the coefficient of specific lethality and \(n\) is the dilution exponent.

Rearrangement of Equation 2 yields

\[
C^n t = - \frac{\log_{10} (N/N_0)}{A}
\]

(8)
In practical disinfection of water, it is usual to find that \( n \) approximates to unity and therefore that the contact period, \( t \), required to inactivate a given percentage of the original population, say 99\%, is proportional to the concentration of disinfectant, \( C \). Equation 8 then becomes:

\[
Ct = K
\]

(9)

where \( K \) = the specific death rate of disinfection.

5.4.2 The C.t concept and the Surface Water Treatment Rule

The USEPA has advocated use of the 'C.t value' (units of \( \text{mg} \text{t}^{-1} \text{min}^{-1} \)) as a way of specifying the degree of treatment necessary to give 99 percent removal as a product of concentration and time. This enable the disinfecting action of different agents and the sensitivities of different micro-organisms to be compared (Hoff 1986, Sobsey 1989). It features in the SWTR (USEPA 1989a) as a system for determining inactivation efficiency for \textit{Giardia} cysts and viruses by reference to tables in a guidance manual (USEPA 1989b). However, strict proportionality of concentration and time for 99\% removal is not always observed and most values of \( n \) have been found to vary between 0.7 and 1.3 for chlorine. The USEPA's (1989b) guidance manual uses an effective value of 0.85 for \( n \) with free chlorine. This was based on an analysis of data for inactivation of the infectivity of \textit{Giardia lamblia} cysts for gerbils and curve fitting by multiple regression (Clark 1990). The equation finally derived for calculation of C.t for free chlorine disinfection to meet the requirements of the SWTR and used in the manual was (Clark and Regli 1991):

\[
C.t = 0.36 \text{pH}^{2.69} \cdot \text{temp}^{-0.15} \cdot C^{-0.15} \cdot [\log(n/n_0)]^{1.00}
\]

(10)

This equation demonstrates the multivariate nature of disinfection. The contact period, \( t \), is the period during which each element or batch of water remains in contact with the disinfectant. Equations 6-10 only hold if (a) the disinfectant is immediately added and completely mixed with the batch of water and (b) if no back or forward mixing takes place during the contact period. This only hold for batches of water held in tanks and is approximated by the flow of water in pipes, long, narrow channels or tanks with baffles giving a serpentine path ("plug flow"). If mixing occurs during contact, a distribution of contact periods will exist and the efficiency of disinfection will be seriously reduced.

In Section 4.6, it has been explained that the C.t approach, described in the SWTR (USEPA 1989a) and the Guidance Manual (USEPA 1989b) specifies \( C \) as the effluent concentration of disinfectant and \( t \) as the \( t_{10} \) value, i.e. the time taken for a step addition of tracer at the inlet to reach 10 per cent of its ultimate concentration at the outlet. The USEPA's approach also allows C.t values to be calculated at individual stages throughout the disinfection sequence, including distribution, in order to obtain improved precision of estimates, for example, where there is more than one point of disinfection, or, in distribution, where the effective concentration is changing. This summation of disinfection potential largely overcomes the criticism of Lawler and Singer (1993) that the tracer method tends to be conservative, particularly in plants departing from the ideal plug-flow regime, and thereby imposes higher operating costs.
6. CHEMICAL TOXICITY

6.1 Characteristics

The health effects of chemicals on people drinking water are of two kinds, acute chemical poisoning and long-term chronic effects.

Acute poisoning results from the sudden release of chemicals into the supply. Like microbial disease, outbreaks are acute, but there is no incubation period and cases cease, once the chemical is removed. The symptoms can be similar to those of bacterial infection. Industrial pollution of the River Dee with phenol in 1984 (Galbraith et al. 1987) resulted in over 500 cases of gastro-enteritis in consumers of water abstracted below the point of discharge. Microbiological cases were excluded epidemiologically. The poisoning species was either phenol or chlorinated by-products produced after chlorination.

The putative hazards from disinfection by-products are cancer, liver damage and blood disorders. Those by-products identified by the USEPA for possible regulation (Regli et al. 1993) are listed in Table 6.1. These effects, unlike those from pathogens, are cumulative, long-term and chronic. They are therefore apparent only in middle and old age. The main immune mechanism is detoxification by the liver.

6.2 Assessment of risks

The cumulative and long-term actions of disinfection by-products render it very difficult to exclude confounding factors from the results of epidemiological and case-history studies. Hence, nearly all information has been obtained by studies on laboratory animals, mainly rats and mice, of strains which are unduly susceptible to cancers (Table 6.1). The procedures are the same as with experimental infectivity (Section 4.4). Groups of animals are fed water containing stratified concentrations of the chemical for a given time, being comparable with the life span of the animal and deleterious effects are noted.

Analysis of risk depends upon the inherent mode of action of the chemical. If a threshold of dose is expected, the tolerable daily intake (TDI) can be derived from the no observed adverse effect level or lowest observed adverse effect level, divided by an uncertainty factor. The TDI is an estimate of the amount in drinking water, expressed as a proportion of body weight, that can be ingested daily for a lifetime without risk to health. In the WHO (1993) Guidelines for Drinking-Water Quality, the guideline values for such compounds were derived by multiplying the TDI by body weight and fraction of the daily input attributable to drinking water. The uncertainty factors were decided for each compound on the basis of expert opinion, and ranged from <10 to 10 000.
<table>
<thead>
<tr>
<th>By-product</th>
<th>Formation by</th>
<th>Health concern and level</th>
<th>Proposed limits</th>
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<td></td>
<td></td>
<td></td>
<td>(µg l⁻¹)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10⁻⁵ risk</td>
</tr>
<tr>
<td></td>
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<td>DWEL b</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(µg l⁻¹)</td>
</tr>
<tr>
<td><strong>By-product</strong></td>
<td><strong>Formation by</strong></td>
<td><strong>Concern a</strong></td>
<td><strong>DWEL b</strong></td>
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<tr>
<td></td>
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<td>(µg l⁻¹)</td>
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</tr>
<tr>
<td><strong>1. Trihalomethanes:</strong></td>
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<td>Cl₂</td>
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<td>B₂</td>
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<td>B₂</td>
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<td>B₂</td>
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<tr>
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<td>Intestinal tumours, rats,</td>
<td>C</td>
</tr>
<tr>
<td>Total</td>
<td>Cl₂, chloramine, O₃</td>
<td>Cancer,</td>
<td>B₂</td>
</tr>
<tr>
<td><strong>2. Haloacetic acids:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichloroacetic acid</td>
<td>Cl₂</td>
<td>Liver tumours, mice,</td>
<td>C</td>
</tr>
<tr>
<td>Dichloroacetic acid</td>
<td>Cl₂, chloramine</td>
<td>Liver tumours, mice,</td>
<td>B₂</td>
</tr>
<tr>
<td>Total bromo- and chloro-</td>
<td>Cl₂, chloramine, O₃</td>
<td>Cancer,</td>
<td>B₂</td>
</tr>
<tr>
<td>By-product</td>
<td>Formation by</td>
<td>Concerna</td>
<td>DWELb (μg l⁻¹)</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------</td>
<td>----------</td>
<td>----------------</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>C₂</td>
<td>Liver damage, mice,</td>
<td>C 56</td>
</tr>
<tr>
<td>Bromate</td>
<td>O₃</td>
<td>Kidney tumours, rats,</td>
<td>B₂ -</td>
</tr>
<tr>
<td>Chlorine</td>
<td>C₂</td>
<td>Kidney toxicity,</td>
<td>D 4000</td>
</tr>
<tr>
<td>Chloramines</td>
<td>C₂, chloramine</td>
<td>Liver damage, mice,</td>
<td>D 4000</td>
</tr>
<tr>
<td>Chlorine dioxide</td>
<td>ClO₂</td>
<td>Brain damage, rats,</td>
<td>D 1000</td>
</tr>
<tr>
<td>Chlorite</td>
<td>ClO₂</td>
<td>Blood damage, cats,</td>
<td>D 350</td>
</tr>
</tbody>
</table>


¹ USEPA classification: B₂ probable human carcinogens, C possible human carcinogens, D inadequate or no human or animal evidence of carcinogenicity.

² Drinking-water effective level.

³ WHO (1993), Guideline Values.

⁴ The sum of ratios of concentrations to guide values for each compound must not exceed 1.

⁵ Provisional guideline value
Many potentially carcinogenic compounds are genotoxic, i.e. they act by inducing mutations in the genetic material of somatic cells. In these cases, there is no threshold dose and the above procedures cannot be used. Some cancers are, however, induced by an indirect means and display a threshold dose response. Where this is established the above procedure can be used to develop guideline values. Otherwise, guideline values must be based upon extrapolation of the data to obtain the estimated concentration in drinking water associated with an excess lifetime risk of cancer. In formulating the WHO (1993) Guidelines, this risk was taken as $10^{-5}$, i.e. one excess case in 100 000 population ingesting the substance at this concentration for 70 years. Concentrations associated with risks of $10^{-4}$ or $10^{-6}$ were obtained by respectively multiplying or dividing the $10^{-5}$ value by 10.

Extrapolation creates uncertainties. Some of these are attributable to the model used for extrapolating processes that are inherently non-linear. WHO (1993) and the USEPA (Regli et al. 1993a,b) both used the linearised multi-stage model and based the guideline value/risk factor on the upper 95 per cent confidence limit of the estimate. Such predictions are conservative, though to a largely unknown extent.

6.3 Basis for legislation

6.3.1 United States

In the United States, the Safe Drinking Water Act (SDWA) requires the USEPA to specify a maximum contaminant level goal (MCLG) for each specified contaminant (see Table 6.1) at a level at which no adverse health effects are expected. The USEPA must also set maximum contaminant levels (MCLs), as close as possible to MCLGs. If it is not technically and economically feasible to monitor for a particular contaminant, then the USEPA must set a treatment technique, in lieu of an MCL, using best available technology. If a compound is known to be carcinogenic when ingested in drinking water, it must be given an MCLG of zero. This represents the differences in approach from WHO’s guideline values for the B2 compounds in Table 6.1. The SDWA presently requires an interim MCL of 100 μg L$^{-1}$ for total trihalomethanes as disinfection by-products. No MCLG is set.

Currently, the USEPA is developing regulations for disinfection and disinfection by-products (Pontius 1993b):

- The Disinfectants - Disinfection By-Products Rule (D-DBPR)
- The Enhanced Surface Water Treatment Rule (ESWTR)
- The Information Collection Rule (ICR)

The first two were discussed in Section 4.6. The ICR will provide data to support development of the D-DBPR and the ESWTR. The D-DBPR will be implemented in two stages with promulgation in 1996 and 2000 respectively but is likely to be delayed. The
anticipated limit values are shown in Table 6.2. The Stage 1 rule will set treatment techniques for removing precursors of disinfection by-products, expressed as total organic carbon. If ozone or chlorine dioxide is used as a pre-oxidant, C.t credit may be given for its disinfection.

Table 6.2  Anticipated maximum contaminant levels (MCLs) and goals (MCLGs) for disinfection by-products in the Disinfectants Disinfection By-Products Rule (Pontius 1993b)

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>MCLG (µg l⁻¹)</th>
<th>Stage 1 MCL (µg l⁻¹)</th>
<th>Stage 2 MCL (µg l⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromate</td>
<td>0</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Chlorite</td>
<td>300</td>
<td>1000</td>
<td>-</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total trihalomethanes</td>
<td>-</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>Chloroform</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bromoform</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bromodichloromethane</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dibromochloromethane</td>
<td>60</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Five haloacetic acids*</td>
<td>-</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Dichloroacetic acid</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Trichloroacetic acid</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* monochloro-, dichloro-, trichloro-, monobromo- and dibromoacetic acids
- not specified

6.3.2  The European Union and the UK

The Drinking-Water Directive 80/778/EEC has specified a guide level for organochlorine compounds, i.e. those not pesticides, of 1 µg l⁻¹ but no maximum admissible concentration (Parameter 32), commenting that, "Haloform concentrations must be as low as possible." The UK’s Water Supply (Water Quality) Regulations (Statutory Instrument 1989) require that the three-monthly average of total trihalomethanes must not exceed 100 µg l⁻¹ (Section 3(2)(e)) in water supplied to consumers.

The draft Proposal revising the Drinking Water Directive (CEC 1995) has set, for water leaving the treatment works, parametric values for chloroform (40 µg l⁻¹) and bromodichloromethane (15 µg l⁻¹), which, where necessary, may be varied to 30 and 25 µg l⁻¹ respectively. These exceed the values of 6 and 20 µg l⁻¹ respectively, representing a calculated excess lifetime risk of 10⁻⁸ for cancer. The Commission has recognised that these values can be difficult to achieve in practice and, in the interests of not compromising disinfection with chlorine, has proposed the parametric values given above.
6.3.3 The views of the WHO (1993) Guidelines

The WHO's (1993) Guidelines set guideline values for individual disinfection by-products, based upon an excess cancer risk of $10^5$ over a lifetime, or on the tolerable daily intake approach, and give full details and reasons for each compound, so that individual water regulators can decide which values and compounds may be of greater or lesser value in setting national standards. The point is made that whenever local circumstances require a choice to be made between meeting either microbiological guidelines or those for disinfectants, or their by-products, the microbiological guideline must always take precedence and where necessary, a chemical guideline value can be adopted, corresponding to a higher level of risk. Efficient disinfection must never be compromised (Guidelines, p93). It also notes the evaluation of the International Agency for Research on Cancer (IARC 1991), which noted that the evidence for association between drinking water containing by-products of chlorination and cancer was considered inadequate and therefore that chlorinated drinking water was, “not classifiable as to its carcinogenicity to humans (Group 3)”.

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7. **THE USEPA’s STRATEGIES FOR BALANCING MICROBIAL AND CHEMICAL RISKS**

7.1 **Quantifying microbial and chemical risks**

The techniques used have been discussed in Section 4.5.5, i.e. the fitting of data from infectivity experiments to the β-Poisson model to determine infective response for a variety of pathogens and prediction of infection, illness and mortality rates for different numbers of pathogens in drinking water in a multiplicative model (Regli et al. 1993a). The scope of the modelling exercise is shown in Table 7.1. The numbers of combinations of pathogens and conditions precludes the presentation of all the predictions. The results are presented by Regli et al. (1993a) but there are some inconsistencies in his tabulated data which do not affect the arguments which follow.

**Table 7.1** Scope of the USEPA’s modelling of microbial risks (Regli et al. 1993a)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Scope of calculations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogens considered</td>
<td><em>Giardia, Entamoeba histolytica</em>, rotavirus, Hepatitis A virus (assuming infectivity of rotavirus and of poliovirus). Data for infectivity derived from published infectivity trials with humans.</td>
</tr>
<tr>
<td>Exposure</td>
<td>Daily exposure to source water containing 1-1000 pathogens / 100 litre for <em>Giardia</em>, otherwise 0.1-100/litre in decimal increments. Consumption 2 litre/day.</td>
</tr>
<tr>
<td>Rates</td>
<td>Daily and annual; annual rates compounded over 365 days = 1 - (1 - daily probability)^365, except Hepatitis A mortality. Illness rates; <em>Giardia</em> and <em>E. histolytica</em> 50% infection rates, rotavirus 55%, Hepatitis A 75%. Death rates: <em>Giardia</em> 0.0001% of illness, <em>E. histolytica</em> 0.3%, Hepatitis A 0.6%, rotavirus 0.01%.</td>
</tr>
<tr>
<td>Water treatment</td>
<td>Raw water, water filtered to remove 2 log units of pathogens, water filtered and disinfected to remove 3 log units of protozoa and 6 log units of viruses. Illness rates calculated at first customer and whole system (rates of infection for protozoa 10% those at first customer, for viruses 1%) assuming filtration and disinfection without failure, with total plant failure on 0.5-100% of time and with total treatment reduced to 2 log units removal on 0.5-100% of time.</td>
</tr>
</tbody>
</table>
Risks of consumers contracting cancers from daily exposure to four disinfection by-products (chloroform, bromoform, bromodichloromethane and dichloroacetic acid) were also calculated as maximum likelihood estimates, based upon animal bioassays and application of the linearised multistage cancer risk assessment model and consumption of 2 litres per person daily. The maximum likelihood estimates are based upon the control tendency of the dose-response curve and therefore give better estimates of incidence than the upper 95 percentile confidence interval.

Some of the predictions from Tables 1 (raw water), 7 (treated, disinfection water, no failure) and 8 (cancer) of Regli et al. (1993a) are presented in Figures 7.1 and 7.2. The predictions are of annual death rates per million consumers for cancers contracted from the four disinfection by-products, compared with death rates per million from four infectious diseases assuming consumption of raw water containing the pathogens (Figure 7.1) and water treated to reduce the pathogens by the amounts given in Table 7.1 by filtration and disinfection as in the SWTR. The outcome of death is chosen here, since this is the usual sequel to cancer and provides the only point of comparison between chemical and microbiological effects of disinfection by chlorine. On both figures, the guideline values using $10^3$ risk value for the potential carcinogens for the four by-products are shown as closed circles (WHO 1993). Regli et al. (1993a) remark that the risk assessment for dichloroacetic acid is being reconsidered by the USEPA and will probably result in lower values than shown in the figures.

Because of the multiplicative exposure models, the prediction curves in Figures 7.1 and 7.2 are linear (as a log-log plot) and those for the by-products and for pathogens have a constant slope at low concentrations. The vertical separations of the curves, for any selected concentrations of pathogens and by-products indicate the difference in risk multiplicatively. The main conclusions to be drawn are:

1. Regli et al. (1993a) present the results of surface water monitoring for Giardia cysts in the US, which show a median concentration of 75 per 100 litres (LeChevallier et al. 1991). At this level, the predicted risk of death from giardiasis is about 250 times less than that from cancer through exposure to the trihalomethanes at their guideline values.

2. The risks of death from amoebic dysentery (E. histolytica) or viral infection, when drinking raw water containing 100 pathogens per 100 litres, is about one million times that from cancer from drinking treated water containing the trihalomethanes at their guideline values.

3. If filtration and disinfection remove pathogens by the extent required by the SWTR, the risks of death from parasitic infections are reduced by 3-4 orders of magnitude (log$_{10}$ units) and of viral infections by 6-7 orders.

4. Although filtration and disinfection reduce the risks of death from infectious disease very considerably, it is not possible to ‘balance’ the risks against those from disinfection by-products in chlorinated water without knowing the concentrations of pathogens in the raw water, their infectivity and virulence and their identity.
5. Because the health risks vary widely for pathogens and by-products, no overall balancing of risks is possible, except for single pairs of pathogen and by-product. Although not shown in Figures 7.1 and 7.2, Regli et al. (1993a) considered the effects upon microbial risks of different frequencies of total and partial (reduction of pathogens by 2 log units) failure of treatment and disinfection. It may be deduced that the risks were correspondingly intermediate between those of the two figures.

7.2 The Disinfection By-Product Regulatory Analysis Model (DBPRAM)

The USEPA is currently concerned with definition of ‘best available technologies’ (BATs) for achieving its regulatory maximum contaminant levels (MCLs) for disinfection by-products, i.e. those achieving the desired result at least cost, while also achieving microbiological treatment objectives, such as those of the SWTR, the coliform rule or any others which may be defined. It has devised a risk assessment model, DBPRAM to carry out this analysis (Regli et al. 1993b). The objectives of this model are:

1. To identify the most likely treatments for meeting chemical and microbiological standards (MCLs).
2. To predict the levels of carcinogenic by-products produced by disinfection and their associated risk to consumers.
3. To predict the levels of pathogens in treated and disinfected water and the associated risks of infection.
4. To calculate the costs of meeting the treatment objectives.

The framework of DDBRAM, given by Regli et al. (1993b, Figure 1) is reproduced as Figure 7.3. The key inputs and outputs are:

- Microbial occurrence in raw water, e.g. *Giardia* cysts.
- Raw water quality (hardness, alkalinity, pH, temperature, turbidity, total organic carbon, ultraviolet absorbance at 254 nm, bromide).
- Microbial occurrence in treated water.
- Concentrations of total trihalomethanes and haloacetic acids after disinfection.
Figure 7.1 Maximum likelihood estimates of annual deaths from infection by pathogens in raw water or of cancers from disinfection by-products in filtered, disinfected water (Regli et al. 1993a). Assumptions of Table 7.1. WHO (1993) guideline values shown by closed circles.
Figure 7.2 Maximum likelihood estimates of annual deaths from infection by pathogens or cancers from disinfection by-products in drinking water (Regli et al. 1993a). Assumptions of Table 7.1. WHO (1993) guideline values shown by closed circles.
Figure 7.3 Framework of the USEPA's disinfection by-product regulatory analysis model, DBPRAM (Regli et al. 1993b)
The model has (Lefikiewicz et al. 1992) three main components, as shown in Figure 7.3:

1. Creation of sets (e.g. of 100 plants) of simulated water supplies, representative of raw water conditions likely to be encountered by suppliers nationally and treatments applied.

2. A water treatment plant model, using the output from the first component which calculates the levels of disinfection and of by-products produced in meeting the SWTR, taste and odour constraints and corrosion control under the lead rule (Pirnie 1992).

3. Aggregated risk assessment based on predicted levels of disinfection by-products and pathogens produced in the water treatment plant model. This assessment extends the trihalomethanes, haloacetic acids and Giardia cysts, information on other hazards being inadequate (Figure 7.3).

Examples of the results of modelling are given in detail by Regli et al. (1993b). Because of the assumptions made and the wide confidence limits of the estimates, it is better to search for general principles and trends rather than to give specific examples. The main principles explored were to examine the effects of lowering the standards (MCLs) for total (or individual) trihalomethanes and haloacetic acids upon incidences of cancer and giardiasis, to explore whether, or not, creation of an enhanced surface water treatment rule (ESWTR) would be preferable and to ascertain the effects of allowing use of alternative disinfectants to chlorine to achieve the MCLs at least cost. The main conclusions derived by Regli et al. (1993b) were as follows:

1. Reductions in the present MCL of 100 µg l⁻¹ for total trihalomethanes to, for example, 25 or 10 µg l⁻¹ would not result in a proportionate decrease in cancers, but would increase the predicted rates of giardiasis (Table 7.2). These predictions allow for use of alternative disinfectants, and it is assumed that they would be used, rather than more expensive technologies for removing precursors.

2. Under any new, lower MCL value for disinfection by-products, 60 per cent of systems would experience increases of 1000-10 000 extra cases of giardiasis annually per million consumers, with decreases in cancer risk of only 0.1-1 case per million per year.

3. It is not possible to conclude with certainty that the total risks from by-products and pathogens will decrease as a result of systems being required to comply with MCLs for specific trihalomethanes or haloacetic acids.

4. Setting an enhanced surface water treatment rule for removal of pathogens or MCLs for specific by-products might create new risks, by forcing suppliers to use alternative disinfectants to chlorine for which the health risks of by-products are less known, or are unknown.
5. The best overall regulatory strategy for the USEPA may be to set limits for precursors of by-products (e.g. total organic carbon and ultraviolet absorbance), for specific by-products, such as trihalomethanes, haloacetic acids and bromate and pathogens responsive to measures for controlling the quality of raw water. However, until more information becomes available, it remains unclear how to regulate total risk reduction cost-effectively.

**Table 7.2** Predicted case rates from imposing different MCLs for total trihalomethanes in disinfected water, using the disinfection by-product regulatory analysis model, DBPRAM (Regli et al. 1993b)*

<table>
<thead>
<tr>
<th>Annual incidence (per million) for:</th>
<th>Existing, 100</th>
<th>25</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total trihalomethanes MCL (µg l⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Cancers from:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trihalomethanes</td>
<td>1 (24)</td>
<td>0.4 (10)</td>
<td>0.4 (10.4)</td>
</tr>
<tr>
<td>Di- and trichloroacetic acids</td>
<td>44 (139)</td>
<td>26.2 (82)</td>
<td>11.3 (35.3)</td>
</tr>
<tr>
<td>(b) Giardiasis</td>
<td>3300</td>
<td>4950</td>
<td>5830</td>
</tr>
</tbody>
</table>

* Cases are maximum likelihood estimates, with 95% confidence interval in parentheses. Model allows alternative disinfectants to chlorine to be used, if they are cheaper in achieving compliance with MCL.
8. DISCUSSION

8.1 Disinfection by-products and risks from cancer

The IARC (1991) considered that evidence for associating chlorination by-products in drinking water with cancer in humans was inadequate and therefore that chlorinated drinking water was not classifiable as to its carcinogenicity to humans. The reasons for the USEPA's regulatory stance are historic. Trihalomethanes were recognised in the mid-1970s as by-products of chlorination and chloroform was shown to be carcinogenic when administered at high levels to rats and mice. Arguments from extrapolation led to the setting of an exposure limit of 100 μg l⁻¹ for total trihalomethanes in 1979. The process has been extended by the recognition of further chlorinated organic by-products which are carcinogenic to laboratory animals. The proposals for the D-DBPR (Section 6.3.1) are a natural extension of this process and are precautionary, in that individual MCLGs will be set at zero or as low as possible, forcing the technologies of treatment and disinfection to adapt in order to comply.

The case for associating chlorination by-products and cancer has recently been advanced by a meta-analysis of twelve previously published epidemiological studies by Morris et al. (1992). Consumption of chlorinated water, surface water or water with high levels of chloroform were used to represent exposure to by-products of chlorination. The meta-analysis pointed to a positive, exposure-related associated for bladder and rectal cancer, but not for other body organs (Table 8.1). However, the relative risks are small and overall fall into the 'weak' category (1.2-1.5) of Monsori (1980), who noted that such effects were difficult to interpret, being prone to bias through confounding. Confounding is a major problem of controlled epidemiological studies, when the primary effect is weak and results from a secondary factor influencing the effect under study differently in the test group of subjects than in the control group. It can be avoided or neutralised by correct statistical design and careful matching of exposed and control groups at the outset or it can be detected or controlled during analysis by stratification or by use of multivariate analysis. Meta-analysis cannot reveal confounding not recognised in the original studies.

This meta-analysis was published about two months before the International Life Sciences Institute’s (ILSI) Symposium on Safety of Water Disinfection (Craun 1993a) and was commented on by only three of the speakers, two from the USEPA. Murphy (1993) presented a large number of criticisms concerned with the accuracy of transcribing the original published data, the difficulties of deciding which studies to reject or combine within a meta-analysis, the precision of estimating exposure to by-products and the effects which excluding unpublished - and probably negative - studies might have had on the outcome. Farland and Gibb (1993), also of the USEPA, comment on the confounding problem and note that the relative risks are small compared with values found for cancer in other studies, e.g. for dyestuffs workers 10 to 50, for bladder cancer in smokers 2-5.
They point out that the overall values of relative risk for bladder cancer (1.21) and rectal cancer (1.38) would respectively translate into about 4000 and 6500 cases annually in the US, if taken at their face value.

Table 8.1  Meta-analytical analysis of association between bladder and rectal cancer and exposure to chlorinated water (Morris et al. 1992)

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Level of exposure</th>
<th>Relative risk (and 95% confidence intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder:</td>
<td>Low</td>
<td>1.03 (0.85-1.24)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.20 (1.04-1.38)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>1.41 (1.24-1.62)</td>
</tr>
<tr>
<td></td>
<td>All exposures</td>
<td>1.21 (1.09-1.34)</td>
</tr>
<tr>
<td>Rectal:</td>
<td>Low</td>
<td>1.13 (0.61-2.09)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>1.49 (1.10-2.01)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>2.04 (1.18-3.53)</td>
</tr>
<tr>
<td></td>
<td>All exposures</td>
<td>1.38 (1.01-1.87)</td>
</tr>
<tr>
<td>All sites:</td>
<td></td>
<td>1.15 (1.09-1.20)</td>
</tr>
</tbody>
</table>

NS - not statistically significant
Relative risk = risk in exposed group/risk in control group.

Pike et al. (1993) noted that, in England and Wales, the life expectancy at birth has increased from 51 years (males) and 55 years (females) in 1911 to 70 and 76 years respectively by 1978, largely by a decrease in non-cancer deaths. The overall age-standardised deaths from neoplastic disease has not changed greatly from 1911, although in the interim period chlorination of drinking water was progressively introduced. The two types of cancer which have increased over this time are lung cancer and leukaemia, neither related to water consumption, while most others have fallen. If the population was exposed to a cocktail of 20 carcinogenic by-products, each presenting a risk of $10^{-4}$, for 70 years (an extreme estimate) the rate would be only about 3 deaths per 100 000 per year, compared with a total incidence for all cancers in England and Wales of 386 per 100 000 for males and 356 for females in 1974, the latest date for which a compilation is available. If the relative risks in the meta-analysis of Morris et al. (1992) are applied to mortality data in the UK, water-related deaths would account for only a small proportion of the 4243 deaths from bladder cancer and 6049 from rectal cancer in 1978.
The summing-up of the ILSI conference (Craun 1993b) was that the information presented did not provide evidence to alter the IARC’s (1992) conclusions about inadequate evidence for the carcinogenicity of chlorinated drinking water for humans.

8.2 The USEPA’s regulatory strategies for controlling risks

The striving for regulation of individual disinfection by-products, required in the developing D-DBPR (Section 6.3.1) leads to the question of over-reaction and the possibility of compromising disinfection. Clark et al. (1993) have commented from the USEPA in this respect:

“Following passage of the Safe Drinking Water Act (SDWA) in 1974 and its 1986 Amendments (SDWAA), the United States water utility industry has found itself in the midst of a revolution that will dramatically change drinking water practices in the United States. For example, the control of potentially carcinogenic disinfection by-products is being considered for SDWA regulation. These by-products result from the interaction of disinfectants, such as chlorine, with natural organic matter in water. A consequence of the proposed action has been increasing pressure on drinking water utilities to minimize the use of chlorine or to consider using alternate disinfectants.

Unfortunately, with attention diverted to this concern over disinfection by-products, the positive recognition due chlorine, as a primary disinfectant in both developed and developing countries, has often been overlooked.

The authors contend that the benefits of using chlorine far outweigh any potential problems associated with disinfection by-products.”

Their analysis of the treatment costs: health benefit ratios for chlorination alone and for conventional treatment with chlorination, for different population sizes were very positive, even under the most conservative assumptions.

The pathogen removal requirements of the SWTR (USEPA 1989) and which will probably be extended to Cryptosporidium in the ESWTR are fixed and are monitored daily under conditions of peak flow by estimating the C.t value across the water treatment and distribution system (USEPA 1989b). It is inevitable that shock loadings of pathogens or poor quality of the source water will result in higher concentrations of pathogens surviving in the water reaching the consumers. It is therefore worth emphasising that the microbiological quality, in terms of pathogen content is not inherently fixed, since the standard is treatment-based. This contrasts with the fixed standards (MCLs) required for disinfection by-products. The two separate concepts for regulating microbial and chemical risks imply that a precise balance of risks to health is not possible theoretically, although it may be approximated over long periods of time in practice.
8.3 The USEPA’s strategies for balancing chemical and microbiological risks

The structure of the DBPRAM and its utilisation to date have been considered in Section 7. It is appropriate to comment upon its capabilities and shortcomings before suggesting either refinements or alternative approaches.

It is heavily dependent upon the methods used for assessing microbial infectivity and risks from by-products of disinfection (Sections 4.5 and 6.2 respectively). Neither can be precisely determined. The calculations of risk then involve estimation of doses and exposure. Constancy of exposure, or average exposure, is implied, whereas concentrations of pathogens and by-products in water and amounts consumed will naturally vary with the individual consumer, with time and from place to place. All are known to be positively skewed in distribution (i.e. approximating to a log-normal distribution) whereas the model will assume randomness. These factors will profoundly affect the relationships between prediction and reality of risk. Such skewness will mean that a small proportion of consumers, fewer than predicted, will be at high risk and that the incidence of illness, infections and neoplastic, will be less than predicted. On the other hand, the reverse will apply to groups who are immuno-deficient.

The risk assessment and by-product calculation parts of the DBPRAM are multiplicative. Therefore uncertainties are multiplied in calculation. No proper overall attempt has been made to calibrate the predictions against known risks. One isolated attempt (Haas 1993) estimated a daily mean risk of viral illness of 0.0168 with 95% confidence intervals of 0.000018-0.2075 (a range of 12 000-fold) from poliovirus infectivity and related it to an observed rate of 0.00082 for viral gastro-enteritis in Montreal by Payment et al. (1991). With such data, the practicability of calibration would seem dubious.

If a multiplicative model cannot be relied upon to be used quantitatively, its general trends can be gauged by inspection, without the need for calculation. One element of DBPRAM allows a decision to be made on allowance of alternatives to chlorine, on grounds of cheaper cost. Such interactive stages cannot readily be predicted by inspection and therefore the model must be run with a number of different assumptions in the input.

The point has already been made that differences in infectivity of different pathogens and of risks of cancer from different by-products make it impossible to achieve a balancing of risk, apart from individual pairs of pathogens and by-products or very generally as a whole.

The real value of a model like DBPRAM is that it will enable a qualitative, rather than a quantitative, assessment to be made of the effects of regulatory changes on risks to health and of costs of compliance and to detect process-cost interactions.
8.4 The way forward - prospects for alternative approaches

8.4.1 Why model?

The main aim of this report has been to review the USEPA’s developments in modelling chemical and microbiological risks. But some questions must also be asked:

1. What is the point of modelling?
2. Is it possible to balance chemical and microbiological risks?
3. What are the needs of the UK’s regulators and would they best be served by the USEPAs approaches to modelling risks?

The needs of the USEPA are clear. The Safe Drinking Water Act and, with it, the SWTR have set maximum contaminant level goals (MCLGs) related to maximum allowable rates of disease, defined by this legislation. The counterbalancing nature of the needs to control disease from waterborne pathogens and disinfection by-products has posed a dilemma, for which modelling to optimise risks appeared to provide a solution. This review has, however, revealed the following conclusions, which do not resolve the dilemma but doubtlessly increase it:

1. The precision of the risk analyses are very poor and their accuracy is unknown since it is, in general, not possible to calibrate the model, because very little data is available from surveillance of disease.
2. Because the basis of risks from by-products are the worst estimates from extrapolation from experiments with mice and other small animals, the MCLGs are unrealistic.
3. There is little convincing evidence that drinking water contaminants are a significant cause of human cancer.
4. Because estimates of risk from individual pathogens and by-products differ, balancing of risks can only be obtained for individual pairs of pathogens and compounds.
5. Setting tighter MCLs for by-products will not reduce cancer levels significantly but will compromise disinfection and protection from infectious disease.

The need of the UK’s regulators (i.e. the Drinking Water Inspectorate of the Department of the Environment in England and Wales) is specifically to ensure that drinking water quality conforms to the requirements of the Water Supply (Water Quality) Regulations 1989 (Statutory Instrument 1989) and amendments and thereby those of the drinking water Directive 80/778/EEC and any future revision (Section 6.3.2). The need for
research or other investigative action can be determined from surveillance of water quality under the provisions of the Water Act 1989, how consolidated in the Water Industry Act 1991 and the Regulations, including the infringements and from surveillance of waterborne diseases by the Communicable Disease Surveillance Centre.

The best use of the modelling approach would seem to be as an exploratory tool, used qualitatively to explore the effects of water treatment on quality and thereby risk. The most valuable use would be in the search for the effects of interactions which might not be obvious from inspection - but this supposes that factors are investigated which might be supposed to interact, such as costs of treatment and population sizes, or pathogen/faecal indicator bacterial levels and biological treatment stages involving predation. Otherwise, modelling using imperfect assumptions would seem to be less useful in terms of output than traditional evaluations of processes to obtain data on their efficiencies and operating costs.

Refinements in microbiological risk analysis are already being reviewed by WRc under contract to DoE (Review of Microbiological Risk Assessment and Drinking Water Supplies; Contract Reference EPG 1/9/17). Some of the factors under study are:

- Levels of pathogens in source water
- Degree of removal of pathogens during treatment
- Review of approaches to risk modelling world-wide
- Consideration of secondary transmission, lack of acquired immunity and other routes of transmission
- Estimating exposure
- Obtaining alternative data from real outbreaks of waterborne disease to supplement experimental infections
- Use of uncertainty analysis, e.g. Monte Carlo methods
- Consider that pathogens are clustered in their statistical distribution in a supply and are not random.

The next two sub-sections discuss some alternative approaches which might well be considered.

### 8.4.2 Attention to the chain of drinking-water treatment

Oxidation or removal of total organic carbon and of inorganic substances (NH$_4^+$, Mn$^{2+}$, Fe$^{2+}$) which react with chlorine and other chemical disinfectants by treatment before terminal chlorination serves a dual role of minimising the formation of by-products and enhancing the rate of disinfection. This removal can be carried out by the following processes:

- Impoundment or bank-side filtration, where the removal mechanisms are partly biological.
- Pre-oxidation, by ozone or chlorine dioxide.
- Biologically active filtration (slow-sand or granular activated carbon).
Removal of the assimilable fraction of organic carbon during treatment also conveys the benefit of controlling microbial growth in distribution and hence the need for maintaining a fairly high residual level of chlorine in distribution, thereby further reducing the formation of by-products.

There is also scope for considering the replacement of chlorination by other disinfection, less likely to result in carcinogenic by-products (Table 6.1).

8.4.3 Alternative approaches to modelling

Disinfection and the natural decay of pathogens in the environment and in water treatment generally follow the first-order, or exponential Chick's Law (Section 5.4, Equation 6), if the concentration or potency of the disinfecting agent remains constant. In practice, this is not always so, as disinfectants combine with substances in water and natural agencies affecting the rate of disinfection vary. If the death rate 'constant' varies randomly, the conditions exist for generating a log-normal distribution of pathogens in the water. It is not surprising, therefore, to find that the distribution of total coliform counts in water supply systems with a history of failure were log-normal (Gale 1994).

The USEPAs modelling has assumed randomness in the distribution of pathogens in water and that risks remain constant from day to day. The results are therefore biased by this assumption by over-estimating risks for the general public. This deficiency is being investigated by WRc under the points of Section 8.4.1.

It is also worthwhile considering what factor of safety is inherent in the requirement for faecal coliforms (Escherichia coli in Report 1995) to be absent in 100 ml samples. This has partly been investigated by WRc (Gale 1994), in investigating the underlying frequency distributions for total coliform bacteria in certain distributions with a history of recurrent failure. It might also be deduced collectively from the annual reports of water undertakers to the Drinking Water Inspectorate, if the underlying statistical distribution can be assumed. A relationship with the occurrence of pathogens and therefore of likely risk of illness will require assumptions to be made about the relative frequencies of faecal indicator bacteria and pathogens.

Another task might be to investigate the cost/benefit relationships from reduction in infectious disease from imposing successive levels of disinfection and other barriers to the transmission of infection, thus providing a justification. Reduction in pathogens by treatment and disinfection follows the exponential decay law (Chick 1908) and the three models of infection (Section 4.5) are also non-linear. Perception of effects by the population tend to be non-linear and are often exponential (common examples are of size and of loudness of noise). From the point of view of an administrator, this may also apply to perception of risk. For example, a single case of illness may be seen as an unfortunate chance (not distinguishable from background), 2-10 related cases, a cluster warranting official concern and the calling-in of epidemiological services, but 10-100, a full-scale outbreak occasioning considerable public alarm. Viewed in this way, the reduction in risk from infection by Shigella dysenteriae (the dose-response curve of Dupont et al. 1989 in
Figure 4.1(a) plotted on a log-log scale would indicate an increasing degree of perceived benefit (reduction in risk) for each successive increment of log reduction in count of pathogen (Figure 8.1). It also indicates, as might be supposed, that very little benefit is obtained until treatment and disinfection bring counts of the pathogen below the median infective dose, ID₅₀.

Finally, one of the USEPA’s contributors to the ILSI Symposium on *Safety of Water Disinfection* considered that relatively little public discussion had occurred regarding acceptable risk for microbial illness and that this discussion should be undertaken and incorporated into future regulations (Macler 1993). In particular, how does the public view infectious disease relative to those from by-products or, indeed, against other environmental challenges? This too might be an appropriate recommendation for future consideration.
Figure 8.1 Replotting of infectivity curve for *Shigella dysenteriae* and human subjects (Dupont et al. 1989), with ordinates axis on a log scale.
9. CONCLUSIONS

The conclusions from this review of the USEPA’s approaches to modelling microbial risks and the formation of disinfection by-products in water are as follows:

1. The USEPA’s regulatory policies for controlling microbial and chemical risks from drinking water derive from the definition of maximum allowable rates of illness and derived maximum contaminant levels goals associated with them.

2. The need to reduce risks from infectious disease by treatment and disinfection to the levels required in the C.t requirements of the Surface Water Treatment Rule has been perceived to be in conflict with the increased risks of cancer from consumption of the resulting disinfection by-products. This has prompted much effort into modelling the two effects to see if a balance can be effected.

3. In constructing the models for risks from pathogens and by-products and for the production of by-products from disinfection, very many assumptions have been made. Because the models are multiplicative, uncertainties are thereby multiplied. The models are therefore valid for qualitative studies and sufficient data are not available to permit them to be calibrated.

4. The modelling has established in very general terms that treatment and disinfection to meet the requirements of the Surface Water Treatment Rule will reduce the microbiological risks of drinking raw water by several orders of magnitude to levels comparable with those assessed by the USEPA for cancer from disinfection by-products at the WHO guideline values. Conversely, tightening the current maximum contaminant levels for by-products will not noticeably reduce cancer levels but could seriously compromise disinfection and protection from waterborne infectious disease.

5. No consistent balancing of risks can be achieved. This is because the levels of pathogens and of precursors of disinfection by-products in raw water vary and because the inherent risks vary for each pathogen and each compound. The most that can be achieved is a balance for individual pairs of pathogen and compound.

6. The models used are linear, therefore the qualitative results could be obtained by inspection of the equations. The main value of such models might be in detecting the results of possible interactions, such as between costs of alternative disinfections, population size and risks. Their best use is as exploratory tools.

7. There is little convincing evidence that drinking water contaminants are a significant cause of human cancer. On the other hand, there is abundant evidence that failures of water treatment and disinfection have caused serious outbreaks of waterborne infectious disease.
8. In the light of Conclusions 4 and 7, disinfection must never be compromised in an attempt to reduce the perceived risks from disinfection by-products. The prudent course of action to overcome concern is to examine the treatment chain for ways to reduce organic precursors of by-products before terminal disinfection. This will, at the same time reduce their formation, increase the efficiency of disinfection and produce a more biologically stable water, reducing the need for 'booster' disinfection during distribution.

9. There is also scope for considering the efficacy of alternative disinfectants to chlorine, less likely to produce by-products.

10. Some suggestions for alternative approaches to modelling have been presented. These are:

   a) Obtaining better data, more related to UK conditions to provide the underlying assumptions for uncertainty analysis, with statistical distributions reflecting those found in water supply. (This is already being funded at WRc by the Department under Contract Reference No. EPG 1/9/17.)

   b) Determining the factor of safety inherent in the requirement for Escherichia coli to be absent in 100 ml samples of water in distribution.

   c) Examining the cost-benefit relationships of disinfection and other means for imposing additional barriers to the transmission of infection by drinking water.

   d) Conduct an exploration of health concerns by the public and acceptable risks.

DISCLAIMER

The views expressed in this Report are those of the Author and not necessarily those of the Drinking Water Inspectorate or the Department of the Environment.
REFERENCES


