
Section VIII

Risk assessment and regulation

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Zoonotic microorganisms present perhaps the greatest past, present, and future risks to the safety of ambient water and drinking-water. Their worldwide distribution varies and is affected by climate and numerous natural and anthropogenic factors, and some microorganisms are emerging or re-emerging as disease risks. Some of the most significant risk factors include transboundary movements of people, food, and animals and increased intensive food and animal production, waste disposal, and cellular mutations, which ensure that the prevalence venues of these zoonotic microorganisms will continue to expand. Virtually every surface water source and many groundwaters are or will be vulnerable to one or more types of these ubiquitous microorganisms.

Analytical methodologies continue to improve our capabilities to detect and identify zoonotic microorganisms with greater specificity and rapidity and to trace them to their sources. Risk assessment is a useful tool that helps practitioners and regulators to determine the extent and magnitude of

vulnerabilities and the consequences of exposure to specific zoonotic microorganisms in particular populations and to focus control actions at critical points in the chain. Nevertheless, public health protection ultimately requires strict reliance on the basic principles of prevention, traditional sanitary engineering applications, and multiple barrier protection. Hazard analysis and critical control points and water safety plan implementation are valuable anticipatory defensive systems for managing animal/food production facilities and public water supplies.

Regulation has the role of providing water quality and performance targets and ensuring that management practices and monitoring and treatment technologies will be installed and will function consistently. Controls and practices at the source, the feedlot and pastures, function by managing animal health to reduce the possibility that the animals are carriers or breeding grounds and shedding human and animal pathogens in their faeces. Waste collection and management practices reduce the potential for transport of contamination from human or animal sources to ambient waters and groundwaters that may be sources for drinking-water supplies. Filtration and disinfection technologies, when properly designed and applied, will control all known zoonotic organisms at the water treatment plant, but the goal is to utilize preventive management techniques at the source to reduce the challenge at the drinking-water treatment plant. Post-treatment recontamination can be prevented by continuous plant operation, residual disinfection, and distribution system design and maintenance.

Indicator organisms such as *Escherichia coli* and faecal coliforms and water quality measurements such as turbidity, although not perfect, are simple techniques that provide a high level of assurance of performance effectiveness of water treatment and barrier trains.

The ability to distinguish faecal organisms from human and animal sources will provide insights as to the origin of the microorganisms and source protection possibilities; in either case, however, prevention of contamination of the drinking-water will be the operative driving force.

A regulatory perspective on zoonotic pathogens in water

S.A. Schaub

27.1 INTRODUCTION

Human infectious diseases potentially associated with the faecal materials from a wide variety of animals are becoming a greater concern around the world. Humankind continues to rely on more and larger animal herds to feed its populations. In addition, humans are encroaching upon lands and waters once considered to be mainly animal habitats. These factors contribute to a greater opportunity for human exposures to pathogens from animal wastes. As a result, nations are confronted with greater impacts from historically prevalent diseases associated with animals and with new diseases entirely unknown even a few decades ago. While some waterborne pathogens that co-infect and cause disease in animals and humans have been around for decades or centuries (*Giardia lamblia*,

Salmonella typhosa, *Ascaris*), others have recently found their way from animal populations to humans (*Cryptosporidium parvum*, *Escherichia coli* O157:H7, severe acute respiratory syndrome [SARS] coronavirus). Additionally, the close proximity of humans to animals and the customs or eating habits of certain populations have helped lead to co-evolution, jumping of host specificity, or genetic shifts in pathogen virulence factors. Humans are now becoming infected by pathogens that previously were confined to livestock or wild animals (Lassa and Ebola haemorrhagic fever viruses, hantavirus, *Mycobacterium paratuberculosis*).

27.2 NEED FOR REGULATORY APPROACHES TO CONTROL ANIMAL-BORNE PATHOGENS

Governments in economically developed societies are expected to play a role in the environmental control or the development and use of water or waste treatments to prevent human infectious diseases, regardless of their origins. Typically, governments establish criteria, standards, and control or treatment procedures for waterborne contaminants to provide national or regional reductions in pathogens in order to improve the level of health protection for the populace. Also, governments often impose monitoring requirements for specific pathogens or faecal indicators to ensure reduced human exposures to contaminated water. However, a lack of clear data on the likelihood and significance of human infectious diseases from animal faecal contamination of water resources has limited the ability of public health professionals and regulators to provide effective protection. There have not been many validated epidemiological links between human illness and water contaminated by animal sources. Regulators have limited justification to initiate more profound regulatory efforts to control zoonotic sources. As a result, although national, state, and local governments should have a role in the prevention or treatment of contaminated water, they may be paralysed to relative inaction and reactionary health protection policies.

The epidemiology of waterborne diseases has often been a major stumbling block to adequately assessing disease risks. An example is the Milwaukee, Wisconsin, USA, outbreak of cryptosporidiosis in the early 1990s. In that outbreak, the disease that infected a majority of the population of this city was first detected by an observant pharmacist who noted an excessive purchase of antidiarrhoeal medicines by the community. The public health community was not aware that an epidemic was occurring. This outbreak and others have demonstrated the lack of sensitivity and timeliness of our ability to detect outbreaks. Most investigations to provide an assessment of the movement of diseases through communities and to establish the sources of the pathogens have

occurred after the outbreak is well established or retroactively, after the outbreak has passed altogether.

27.3 REGULATORY CONTROL OF WATER RISKS

Zoonotic infectious diseases of faecal origin may contaminate the surface waters and groundwaters that humans use for drinking, recreation, fishing/shellfishing, irrigation, and aquaculture. Currently, animal sources of pathogens are often not specifically considered in possible new regulatory controls to protect waters or prevent human exposures because of the lack of regulatory tools to do so. Different regulatory approaches could be proposed for the future if, for instance, it is determined that there is a significantly reduced risk for human exposure or illness from animal-borne faecal pathogens in water compared with human-derived pathogens. Some of the data requirements and tools for considering zoonotic pathogen sources in future regulations include the following:

- analytical methods to sample, identify, and quantify specific pathogens or faecal indicators, including identification and use in control of animal pollution sources;
- evaluation of treatment effectiveness and health protection targets for discharge permits and total maximum daily loads (TMDLs) for specific contaminants;
- development or revision of protective criteria or standards that will ensure that water uses are protected; and
- improved monitoring strategies for animal-based point and non-point sources.

27.4 EXAMPLES OF REGULATORY APPROACHES

Some examples of current applications of regulations for microbial contaminants in an economically developed country are those of the USA. The approach for the monitoring and control of exposures to microbial hazards is handled differently for drinking-waters than for ambient waters used for other human purposes. The major reason is because drinking is considered a mandatory human water use, while other uses, such as recreation, are considered voluntary uses.

Under the *Safe Drinking Water Act*, the US Environmental Protection Agency (EPA) issues national drinking-water standards, which all public water utilities are required to meet. The standards are called Maximum Contaminant Levels (MCLs). Under current regulations, Maximum Contaminant Level Goals (MCLGs) of “0” are applied for enteric viruses, *Giardia*, and *Cryptosporidium*. However, actual routine monitoring for microorganisms is limited to total coliforms or *E.*

coli because of the high costs of conducting specific pathogen analyses in a routine manner and relatively poor precision and accuracy of analytical methods. The regulations rely on designed efficiency (performance) of the water treatment and disinfection technologies to attain the MCLG in the finished water. Total coliforms are routinely monitored in treated waters, and the detection of a single coliform per 100 ml triggers additional monitoring and the investigation of the treatment system. Repeated “detects” are reported to the states and to the US EPA.

On the other hand, under the *Clean Water Act*, the US EPA provides ambient water quality criteria, which rely on the application of faecal indicator microorganisms at prescribed target levels for health protection dependent on the water’s use (e.g., recreational, shellfish growing and harvesting, and drinking). States adopt the criteria as standards for waters having designated uses that have to achieve a particular level of protection where human exposure is likely. These criteria are used to provide the swimmable and fishable requirements for US waters under section 304(a) of the Act. The US EPA is planning to establish future “drinkable” 304(a) criteria for *Cryptosporidium*. Below is a brief description of some of the essential components of the criteria for recreation and shellfishing:

- Recreational water quality criteria (primary recreation sites):
 - (a) fresh water: 126 *E. coli* or 33 enterococci/100 ml using a running geometric mean over five weekly samples, which provide a protection level of 8 illnesses/1000 swimmer days;
 - (b) marine water: 35 enterococci/100 ml using a running geometric mean over five weekly samples, providing a protection level of 19 illnesses/1000 swimmer days; and
 - (c) single sample maximum values (upper-bound confidence intervals above the mean), which are less protective, but which can be applied at less frequently used recreational areas or in other primary contact venues (e.g., surfing, diving, water skiing).

The recreational criteria numbers were established for two indicators, based upon results of prospective epidemiology studies in which recreational water samples were measured for the indicators and persons bathing (with head immersion) were monitored over a 10-day period after the swimming event to determine if they experienced acute gastrointestinal disease symptoms. In the future, it is anticipated that new criteria and new or improved indicator microorganisms or methods will be based upon a companion study of new rapid indicator methods in conjunction with prospective swimmer epidemiology studies at freshwater and marine beaches.

- Shellfish growing water quality criteria for shellfish beds where the harvest will be sold for raw edible consumption:
 - (a) identify and characterize growing areas; impacts of upstream wastewater treatment systems; required design of treatment system capabilities to protect waters and shellfish; size of shellfish water harvest zones; and treatment plant operation and maintenance procedures to ensure protection of the shellfish use;
 - (b) approved unrestricted shellfish bacteriological quality classification:
 - total coliform: 70 most probable number (MPN)/100 ml (and <10% exceed 230 MPN/100 ml); or
 - faecal coliform: 14 MPN/100 ml (and <10% exceed 43 MPN/100 ml);
 - (c) measure compliance by analysing at least 15 of the most recent adverse pollution conditions (minimum 5 per year) or the most recent 30 systematic random samples (minimum 6 per year) at stations located to evaluate actual or potential sources of pollution; and
 - (d) establish National Pollutant Discharge Elimination System (NPDES) permit levels and monitoring for sewage treatment plants discharging to waters where shellfish may be grown for commercial sale or recreational fishing.

The shellfish criteria also provide additional target levels for waters that may be impacted by higher indicator levels, which may require periodic closures or even requirements for the “relay” or depuration of the shellfish stocks before harvest and sale from restricted waters.

Criteria for recreational and shellfish growing waters, using faecal indicators, have been effective tools to significantly reduce the levels of waterborne gastrointestinal disease. However, there may be shortcomings to the applicability of the criteria if animal sources of faecal waste are to be delineated from human wastes, assuming validation of the premise that human health risks from animal wastes are less than risks from human wastes. Unfortunately, actual human health risks are not well known or measured for the full range of zoonotic faecal-borne pathogens. Finding data that link animal faecal contamination with disease outbreaks from water exposure has been and will continue to be a significant challenge that will complicate future criteria development. Because of the lack of epidemiological evidence directly associating animals with waterborne disease risks, there has not been a concerted effort to determine when, where, or how to control sources or regulate these contaminants or to estimate their relation to human risks for revising criteria. Additionally, epidemiological studies conducted to correlate faecal indicators with disease risks or the pathogens themselves have

not been conducted on waters in which animal contamination is the dominant source for exposure.

Public health policy discussions have recently begun in the USA regarding the significance of animal-borne human pathogens, better definition of their health significance for the water environment, and the potential need to control these contaminants. There are a number of animal-based industries and some public health practitioners who do not think that the magnitude of animal faecal contaminant sources of human pathogens are very important or who believe that the levels of risk are significantly less than if the same pathogens were from human sources. There has also been speculation in the scientific community that animal sources of human pathogens may have less ability to infect and cause disease in humans than a human pathogen source. Possibly, human virulence gene expressions are shut off in pathogens derived from animal hosts. It has been suggested that if animal-borne human pathogens are less likely to cause human infection, then regulations or criteria might be relaxed if animals were identified as the source, while still being protective of human water uses. If regulators can determine the magnitude and distribution of disease risks from animal faecal sources, then it may be feasible to modify health protection targets in standards, criteria, and watershed management. Also, risks may be characterized differently based upon the relative probability of human infectious diseases being present in animal populations. It has been suggested that bacterial and parasitic diseases from animal sources are more likely to be a common human risk than viral diseases because they appear to have a wider range of hosts. This could be an important distinction for possible future regulatory approaches.

Another potentially important scenario exists concerning animal-borne human pathogens. That is, what are the implications of human faecal shedding of the pathogens that co-infect animals? Because of the increased proximity of humans to animals and the magnitude of the human waste load to water, if not adequately treated, this could provide a significant level of pathogens capable of infecting susceptible livestock, pets, and wildlife. Could human waste contamination of waters help maintain zoonotic infections and potential reservoirs for human pathogens, which can be spread to other animals and back again to humans in a cyclical process? This issue may also need to consider the implications of invasive species of pathogens and of animals. Also, cloned animals may need to be considered. Regulators may need to consider these potential ramifications to public health as we gain better data and knowledge about human contributions to zoonoses, the maintenance of infectious disease cycles, and the implications of anthropogenic activities to the health of animal populations.

With respect to the utility of the current US EPA criteria approach using classical indicators, there is also a question about the applicability of the criteria levels. The relationship of indicators and how they represent disease risk may

differ in faeces of various animal species. Some investigators have suggested that various animal species shed significantly different levels of the current indicators (per gram of faeces) than humans. However, it is not known if these differences are large enough to have a serious impact on the reliability of current health criteria or standards to accurately portray the probability of health risks if the targeted levels of indicators are maintained for all contamination sources. Future source tracking technologies, which are described below, may provide monitoring tools to determine the nature of faecal sources.

27.5 ISSUES TO ADDRESS BEFORE ESTABLISHING CONTROLS

Public health officials and regulators need to know the significance of the threats of disease from animal-borne human pathogens, whether from the livestock industry, from pets and feral animals, or from wildlife, in order to provide appropriate source mitigation, determine appropriate levels of treatment, or impose limits on waterborne exposure based on the risks. There are a number of factors that are important considerations in determining the likelihood and significance of the spread of infectious disease organisms from animals to humans and their control or regulation:

- (1) the levels of pathogens released to a body of water and the relative degree of pollution of the water based on the size and strength of the waste source;
- (2) the length of time the pathogen survives in the aquatic environment and the possibility of its growth in that environment (and also its survival relative to potential indicators);
- (3) the effectiveness of available treatment and disinfection technology and practices to reduce or eliminate the pathogens, either at the source or before use of a contaminated water;
- (4) the infectious dose for the pathogens to cause infection and/or disease for the particular exposure envisioned for particular water uses;
- (5) the severity and duration of illness likely to be manifested in the persons exposed from a water use; and
- (6) the effectiveness and longevity of immunity either from vaccinations or from previous exposures to the pathogens.

Each of these factors plays a significant role in the likelihood of infection and disease outcomes. Different factors may have a predominant effect on the outcome for each pathogen. Regulators and public health officials need to develop

a strategy to consider each of these factors in trying to reduce or eliminate the risk of disease to water users. As newly emerging or modified (natural or engineered mutations) pathogens from animal sources emerge as potential water contaminants, there may be increased demands to establish data and new tools, such as:

- analytical methods to determine their sources, environmental fate, and transport;
- applicability of class surrogates or indicators;
- water and wastewater treatability and discharge permits;
- dose–response relationships; and
- monitoring requirements for establishing criteria and standards, TMDLs, and pollutant (water quality) trading.

Regulatory decisions that would need to be considered include determinations of whether the pathogen itself needs to be the analytical target—whether it can be represented by a pathogen class surrogate (a member of a broad group of pathogens; e.g., total enteric viruses) or whether common faecal indicators can be applied. Some lingering problems with direct pathogen or pathogen class analysis are the typically high costs for sampling and analysis, especially for protozoa, viruses, and parasites. Additionally, there are typically greater levels of training, expertise, and laboratory equipment required. However, progress being made in development of molecular methods of analysis may help reduce the costs and complexity of performing direct pathogen monitoring. The advances in multiple array probe technologies may allow simultaneous detection of a wide variety of pathogens in a sample. Still other problems exist with some molecular approaches, in that it is difficult to determine if pathogens in a water sample are dead or alive. Finally, the long time required to sample and perform analyses is a major roadblock, especially where it is important to make a quick determination about whether or not it is safe to use a water, particularly for recreational and crop irrigation uses.

27.6 REQUIREMENTS FOR CRITERIA WHERE ANIMAL PATHOGENS/INDICATORS ARE NEEDED

It is likely that, for years to come, there will be a requirement for sampling and analysis of faecal indicator bacteria from humans and animals. There will also be a need for the development, validation, and application of other indicators for different exposures and diseases associated with water uses. Faecal indicator methods are relatively inexpensive, are easy to learn to use, have “low tech”

laboratory equipment requirements, and typically provide a measure of viability of the organisms in the sample. New research is developing rapid methods that provide results within a few hours. Other research in microbiological source tracking (MST) methods is providing promising new indicator technologies (antibiotic resistance, *Bacteroides* indicator, polymerase chain reaction [PCR] probes, coliphage typing, etc.) that can differentiate faecal sources and have the potential to detect and discriminate human versus livestock versus various wild animal contamination. Other work is evaluating the efficacy of faecal or wastewater chemicals to help discriminate faecal or wastewater sources. Some non-microbial indicators under investigation are faecal sterols, detergents, fabric whiteners, and secretory immunoglobulins. These chemical indicators could be useful as added tools to determine the sources of faecal and wastewater contaminants, and some have the potential to be applied as “dipstick” or on-line monitoring methods.

It is likely that monitoring for enteric disease risks will be more sophisticated in the future than it is today. As technologies develop, it will be possible to use “tiered” monitoring approaches, where cheap, rapid, and even on-line methods would be used for screening water samples. Then, progressively more targeted, sophisticated methods would be used on positive samples to further delineate sources and viability, and even to detect and quantify specific pathogens of concern. Alternatively, a combination of different indicators may be analysed simultaneously in sampling protocols to provide an index of faecal pollution strength and source, similar to other environmental quality monitoring applications (e.g., air quality indices).

There continues to be a real requirement for analytical methods for water, whether for pathogens or indicators, to be used with increased levels of confidence to support regulatory needs to reduce health risks. Historically, new methods to be used in a regulatory context are first validated by outside laboratories to demonstrate that they can be used effectively by someone other than the method developers. Validated methods are then collaboratively tested on the water medium in which they will be used to establish their analytical performance. Collaborative testing of methods typically involves a designated group of qualified laboratories that use a single testing protocol and strictly follow the analytical procedure. Typically, representative subsamples of the water medium (either spiked or unspiked for the microorganisms of concern) made from single preparations of various waters of interest would be distributed to the laboratories from single preparations. The collective multilaboratory sample results are analysed to establish the precision, accuracy, and inter- and intralaboratory bias for use of the method. Often there are predetermined performance goals for acceptance of a new method, which must be met by the collaborative study in order for it to be used in a regulatory setting.

27.7 HEALTH CRITERIA AND STANDARDS SETTING

In setting health criteria or standards for microbial health risks in water in the USA, the selected analytical methods must first achieve required acceptance levels, as described above. Then the method must be experimentally evaluated to establish its relationships to health-protective numerical targets in order to define acceptable occurrence levels for criteria. When there is a requirement for a regulation for a specific pathogen, it may be necessary to conduct human or animal dose–response studies, where the dose administered (quantified by the pathogen method) is evaluated in terms of specific health effects, such as infection or disease end-points. The relationship of measured dose to health effects can then be defined to establish the protective levels required for regulation. On the other hand, for health criteria, health risks are often derived from prospective epidemiology studies or outbreak evaluations, where an indicator method is measured in the water during the time and at the location that the human exposure is occurring. A correlation is sought for the indicator level associated with the acceptable level of a targeted disease syndrome (e.g., acute gastrointestinal disease for recreational criteria).

In the future, regulatory decisions may need to consider the capability we have to detect and discriminate animal faecal pollution from human sources and also the ability we have to determine the relative risks associated with human versus animal-borne pathogens. If risks are not equivalent, then the question becomes what metrics are available that regulators can use to distinguish between the sources or the risks: MST methods; virulence factor activity relationships; or dose–response data that may demonstrate differences in infectivity and disease outcomes for animal versus human pathogen sources. If adequate decision-making tools or methods to achieve the above are not available or feasible, then it may be appropriate to continue to regulate all faecal wastes equivalently, a conservative approach.

The current regulatory approaches that could be applied in the future to better control animal faecal contamination of water and reduce human exposure are as follows:

- (1) reduce contaminants at their sources by on-site treatment of wastes (e.g., concentrated animal feeding operations [CAFO]; NPDES discharge permits) or otherwise deny their entry to ambient water resources;
- (2) reduce human exposure during use of ambient waters by treatment of the water before use (drinking-water source treatment/disinfection); or
- (3) intervene in the use of the contaminated water (e.g., beach and shellfish bed closures).

A number of approaches specific to the protection of drinking-water consumers are available. These could be adjusted to consider different animal faecal contaminant risks to health (if such were demonstrated) to provide significant reductions in treatment requirements while still protecting the health of consumers:

- (1) source water protection programmes;
- (2) source water criteria at intakes, such as the US EPA's consideration of 304a criteria for *Cryptosporidium*;
- (3) modified treatment and disinfection processes and tools to meet water treatment requirements (such as proposed for removing *Cryptosporidium* at the plant under the US EPA's Long Term 2 Enhanced Surface Water Treatment Rule);
- (4) maintenance of the integrity of distribution systems; and
- (5) systematic identification and risk assessment for potentially problematic emerging pathogens, such as the US EPA's Contaminant Candidate List for potential future drinking-water regulation.

There are also a number of approaches to the protection of direct ambient source water uses such as for recreation, irrigation of fruits and produce to be consumed raw, shellfish growing, drinking-water sources, and aquaculture. A major emphasis of protection of these uses is the establishment of discharge permits for animal wastes such as in CAFO and animal feeding operation (smaller-scale animal operations) wastes, but also for rendering plants and abattoirs. TMDLs are applied to protect uses and can consider both point and non-point discharges of animal wastes. A new approach being used for some pollutants in the USA is the application of "pollution trading," whereby one pollutant source with costly treatment requirements could trade pollution "credits" with another source having less costly needs. In the future, these pollution trading approaches could utilize microbiological TMDLs as a tool to meet the trading needs. It will be interesting to see if faecal indicator trading has a place in this overall contaminant management scheme to ensure that infectious disease levels are kept in check.

Most economically developed countries have ambient water criteria for various water uses to protect their populations from infectious disease. There are efforts to look at new ways to apply criteria to uses. In the USA, the EPA is looking at the establishment of integrated microbiological criteria wherein a single criteria approach and a set of faecal indicators (or pathogens) are monitored for all ambient water uses. In this integrated application, the acceptable health criteria levels for the uses may be different, but the indicators or pathogen methods could be standardized. This approach could also apply tiered monitoring methods and

faecal pollution indices (based upon several different indicators considered together to establish a numerical index of contamination levels).

Any new approaches to monitoring discharge permits, non-point sources, TMDLs, or ambient criteria to discriminate animal-borne human pathogens may need to rely on improved or new methods to implement discriminatory approaches to animal contaminants. A number of analytical methods for monitoring these various water-based regulatory needs are being investigated. New molecular methods such as PCR, reverse transcriptase-PCR, Multiplex probes, and various immunological and biochemical techniques for specific pathogens or pathogen classes are being developed and evaluated for their efficacy to detect, identify, quantify, and even determine the presence of pathogen virulence factors. Also, improved molecular methods for microbial indicators of faecal contamination are being developed. Within the realm of indicator methods is the current US EPA focus on validation of rapid (<2 h) methods to detect and quantify faecal contamination levels. The availability of rapid methods would be a significant improvement as tools for real-time NPDES monitoring and for ambient water quality monitoring, where rapid data availability could influence decisions on treatment requirements and on safety of water uses.

A number of analytical methods have been identified that have capabilities to discriminate (to various degrees) animal versus human faecal contamination. MST methods are mostly in the development and evaluation stage. Some methods rely on antibiotic resistance patterns; others are direct measurements of specific pathogens or new indicators, such as coliphage and *Bacteroides* sp. bacteria; but most rely on molecular techniques, such as PCR probes of specific unconserved areas of the genome and immunological or biochemical techniques that determine differences in the genotypic or phenotypic expression of indicators/pathogens. There has been an attempt in the USA (private sector and US EPA-funded) to establish a prescribed set of protocols to evaluate the efficacy of the MST methods. A major hurdle may be the inability of the methods to work adequately in discriminating sources beyond a single watershed or geographical region. To be useful as regulators' tools, the source tracking methods will need to be capable of providing at least regional or preferably national capabilities to discern differences in animal versus human faecal contamination sources.

27.8 CONCLUSIONS

Strong epidemiological evidence that animal-borne human faecal pathogens are a significant risk for human exposure in faecally contaminated water is lacking. There is a need for more data to make informed scientific judgement about the significance and magnitude of zoonotic faecal pathogens as agents of human infection from contaminated water. Until there is adequate evidence for or against

the concept of quantifying different risks, it will not be possible to alter regulatory approaches that would consider animal faecal contaminant sources as different from human sources.

Currently, animal-associated human pathogens are not discriminated from human sources for various water uses, such as recreational, shellfishing, and drinking-water source waters. Additionally, microbial indicators of faecal contamination do not differentiate between human and animal sources. Targeted research efforts are needed to provide discriminatory analytical tools to help advance regulation if they are warranted.

There are a number of data gaps regarding the adequacy of approaches for monitoring and analysis in criteria and standards setting, as well as a need to validate and standardize current and new methods. For animal pathogen sources, it is necessary to establish whether or not pronounced differences exist for exposures to animal faecal sources; environmental fate and transport of zoonotic pathogens; their treatability in drinking-water and wastewater; differences in the infectivity and virulence of zoonotic pathogens for humans; dose-response; and epidemiological correlations. Also, there is a need to determine if animal-borne pathogens are adequately covered under current regulations and treatment approaches, as well as determining what the appropriate indicators are.

Current research efforts may allow regulations in the future that will incorporate the ability to discriminate animal faecal sources from each other and from human sources based upon MST. These technologies may have promise for use in better defining TMDLs and possibly for implementing pollution trading approaches.

27.9 REFERENCES

- Clean Water Act* (1987) US Code of Federal Regulations vol. 33, Amended by the Water Quality Act of 1987 (PL 92-500).
Safe Drinking Water Act (1996) US Code of Federal Regulations vol. 42, 1996 Amendments (PL 104-182).

28

The Stockholm framework for guidelines for microbial contaminants in drinking-water

R. Carr and J. Bartram

28.1 INTRODUCTION

Following a major expert meeting in Stockholm, Sweden, the World Health Organization (WHO) published the document *Water Quality: Guidelines, Standards and Health; Assessment of Risk and Risk Management for Water-related Infectious Disease*. This document creates a harmonized framework for the development of guidelines and standards, in terms of water-related microbial hazards (Fewtrell and Bartram 2001). This framework involves the assessment of health risks prior to the setting of health targets, defining

© World Health Organization (WHO). *Waterborne Zoonoses: Identification, Causes and Control*. Edited by J.A. Cotruvo, A. Dufour, G. Rees, J. Bartram, R. Carr, D.O. Cliver, G.F. Craun, R. Fayer, and V.P.J. Gannon. Published by IWA Publishing, London, UK. ISBN: 1 84339 058 2.

basic control approaches, and evaluating the impact of these combined approaches on public health status (Figure 28.1).

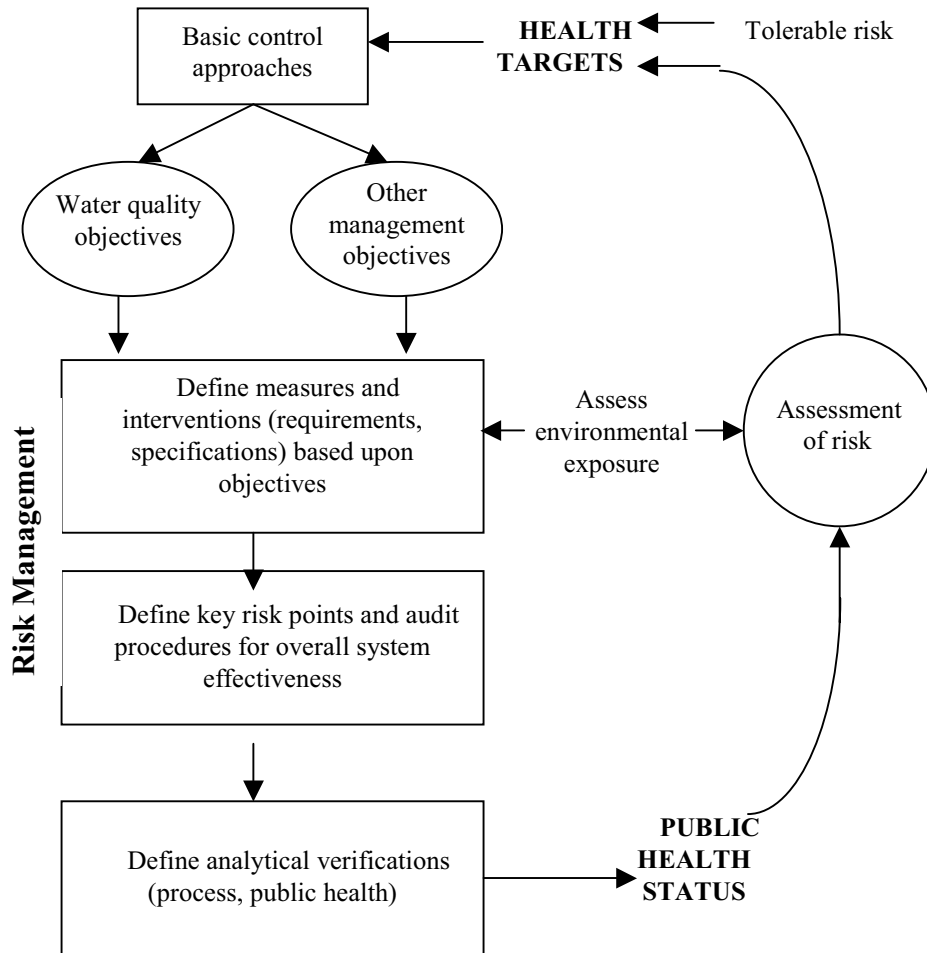


Figure 28.1. Stockholm framework for assessment of risk for water-related microbial hazards (from Bartram *et al.* 2001).

The framework allows countries to adjust guidelines to local social, cultural, economic, and environmental circumstances and compare the associated health risks with risks that may result from microbial exposures through wastewater use, drinking-water, and recreational/occupational water

contact (Bartram *et al.* 2001). This approach requires that diseases be managed as a whole package and not in isolation. Comparisons can be made between disease outcomes from one exposure pathway or between illnesses by using a common metric, such as disability-adjusted life years (DALYs).

Future WHO water-related guidelines will be developed in accordance with this framework. This chapter contains a summary of the framework components (Table 28.1) and a discussion of DALYs and tolerable risk. For a more detailed discussion of the framework, see Fewtrell and Bartram (2001).

Table 28.1. Elements and important considerations of the Stockholm framework (adapted from Bartram *et al.* 2001)

Framework component	Process	Considerations
Assessment of health risk	Hazard assessment	Best estimate of risk — not overly conservative
	Environmental exposure assessment	Equivalence between risk of infection and risk of disease
	Dose–response analysis	Health outcomes presented in DALYs, facilitates comparison of risks across different exposures and priority setting
	Risk characterization	Risk assessment is an iterative process — risk should be periodically reassessed based on new data or changing conditions
Tolerable risk/health targets	Health-based target setting based on risk assessment Define water quality objectives	Risk assessment is a tool for estimating risk and should be supported by other data (e.g., outbreak investigations, epidemiological evidence, microbiological risk assessment, and studies of environmental behaviour of microbes)
		Process dependent on quality of data
		Risk assessment needs to account for short-term under-performance
		Needs to be realistic and achievable within the constraints of each setting
		Set based on a risk–benefit approach, should consider cost-effectiveness of different available interventions
		Should take sensitive subpopulations into account
		Index pathogens should be selected for relevance to contamination, control challenges, and health significance (it may be necessary to select more than one index pathogen)

Framework component	Process	Considerations
Risk management	Based on health-based targets: Define other management objectives Define measures and interventions Define key risk points and audit procedures Define analytical verifications	Risk management strategies need to address rare or catastrophic events A multiple-barrier approach should be used Monitoring — overall emphasis should be given to periodic inspection/auditing and to simple measurements that can be rapidly and frequently made to inform management Hazard analysis and critical control points (HACCP)-like principles should be used to anticipate and minimize health risks
Public health status	Public health surveillance	Need to evaluate effectiveness of risk management interventions on specific health outcomes (through both investigation of disease outbreaks and evaluation of background disease levels) Procedures for estimating the burden of disease will facilitate monitoring health outcomes due to specific exposures Burden of disease estimates can be used to place water-related exposures in the wider public health context to enable prioritization of risk management decisions Public health outcome monitoring provides the information needed to fine-tune risk management process through an iterative process

28.2 DISABILITY-ADJUSTED LIFE YEARS (DALYS)

DALYs are a measure of the health of a population or burden of disease due to a specific disease or risk factor. DALYs attempt to measure the time lost because of disability or death from a disease compared with a long life free of disability in the absence of the disease. DALYs are calculated by adding the years of life lost to premature death (YLL) to the years lived with a disability (YLD). YLL is calculated from age-specific mortality rates and the standard life expectancies of a given population. YLD is calculated from the number of cases multiplied by the average duration of the disease and a severity factor ranging from 1 (death) to 0 (perfect health) based on the disease (e.g., watery diarrhoea has a severity factor ranging from 0.09 to 0.12, depending on the age group) (Murray and Lopez 1996; Prüss and Havelaar

2001). DALYs are an important tool for comparing health outcomes because they account for not only acute health effects but also delayed and chronic effects, including morbidity and mortality (Bartram *et al.* 2001). When risk is described in DALYs, different health outcomes can be compared (e.g., cancer vs. giardiasis) and risk management decisions can be prioritized.

28.3 WHAT IS AN ACCEPTABLE (TOLERABLE) RISK?

According to Hunter and Fewtrell (2001), the following criteria can be used to judge whether a risk is acceptable:

- it falls below an arbitrary defined probability;
- it falls below some level that is already tolerated;
- it falls below an arbitrary defined attributable fraction of total disease burden in the community;
- the cost of reducing the risk would exceed the costs saved;
- the cost of reducing the risk would exceed the costs saved when the “costs of suffering” are also factored in;
- the opportunity costs would be better spent on other, more pressing public health problems;
- public health professionals say it is acceptable;
- the general public says it is acceptable (or, more likely, does not say it is not acceptable); or
- politicians say it is acceptable.

Tolerable risks are not necessarily static. As tools for managing water-related disease transmission improve, levels of risk that are tolerable may decrease. Tolerable risks can therefore be set with the idea of continuous improvement. For example, smallpox was eradicated because it was technologically feasible to do so, not because of the continually decreasing global burden of disease attributed to this disease.

The control of *Listeria monocytogenes* in ready-to-eat food products provides another example. *Listeria* causes listeriosis, a serious, although rare, foodborne disease (Codex 1999). In the 1980s, effective management procedures were developed that demonstrated that finished, ready-to-eat food products could be produced with very little or no *Listeria monocytogenes* present. In the USA, a policy of “zero” tolerance for *Listeria* in these products was adopted. As a result of the implementation of this policy, the incidence of and mortality due to foodborne listeriosis in the USA declined by 44% and 49%, respectively, over a period of 4 years (Billy 1997). In many developed countries, similar reductions in foodborne listeriosis cases (99% of listeriosis is estimated to be foodborne; Mead *et al.* 1999) have occurred due to adoption of good management practices and HACCP programmes by food processors,

improvement of the integrity of the cold chain in storage/transport, etc., and better risk communication to susceptible consumers (Codex 1999).

28.4 TOLERABLE MICROBIAL RISK

For water-related exposures, WHO has determined that a disease burden of 1×10^{-6} DALYs per person per year from a disease (caused by either a chemical or infectious agent) transmitted through drinking-water is a tolerable risk (WHO 2004). This level of health burden is equivalent to a mild illness (e.g., watery diarrhoea) with a low case fatality rate (e.g., 1 in 100 000) at approximately a 1 in 1000 annual risk of disease (10^{-3}) to an individual (a 1 in 10 risk over a lifetime) (WHO 1996, 2004; Havelaar and Melse 2003). The US Environmental Protection Agency (EPA) sets a tolerable risk in relation to infection, rather than disease, of less than 1 *Giardia intestinalis* infection in 10 000 people per year (a 10^{-4} risk) from drinking-water (Regli *et al.* 1991). However, based upon background rates of gastrointestinal disease in the general population, Haas (1996) argued that an acceptable risk of infection of 10^{-4} per person per year was too low and that even a risk of infection of 10^{-3} per person per year was too low.

The US EPA set the tolerable risk level using the risk of infection rather than the manifestation of disease. This is an important distinction, because there are a number of factors that determine whether infection with a specific pathogen will lead to a disease, including the virulence of the pathogen and the immune status of the individual (see Prüss and Havelaar 2001 for a further discussion of infection versus disease). For example, hepatitis A infections in children are predominantly asymptomatic (no apparent symptoms), but the same infection in adults often does lead to disease symptoms (WHO 2000). Asymptomatic infection can be confirmed by microbiological examination of stool specimens and in some cases by detection of a serological response (Teunis *et al.* 1996). However, infection is harder to detect in the general population because there are no obvious disease symptoms to track. For this reason, it is more difficult to measure compliance with and/or enforce a guideline value set with infection as an end-point compared with one based on disease, and such a guideline value is less precise in terms of public health protection.

Tolerable risk can be looked at in the context of total risk from all exposures, and risk management decisions can be used to address the greatest risks first. For example, it would have very little impact on the disease burden if the number of cases of salmonellosis attributed to drinking-water are halved when 99% of the cases were related to food.

For water-related exposures to microbial contaminants, diarrhoea or gastrointestinal disease is often used as a proxy for all waterborne infectious diseases. Mead *et al.* (1999) estimated that the average person (including all age groups) in the USA suffers from 0.79 episodes of acute gastroenteritis (characterized by diarrhoea, vomiting, or both) per year (a 7.9×10^{-1} annual risk of gastrointestinal illness). The rates of acute

gastroenteritis among adults worldwide are generally within the same order of magnitude (Table 28.2). However, children — especially those living in high-risk situations, where poor hygiene, sanitation, and water quality prevail — generally have a higher rate of gastrointestinal illness. Kosek *et al.* (2003) found that children under the age of 5 in developing countries experienced a median of 3.2 episodes of diarrhoea per child per year (a risk of 3.2 per year).

Table 28.2. Diarrhoea cases per year by age group and country income level (adapted from Murray and Lopez 1996)

Age (years)	Country income level ^a		
	Low	Middle	High
0–4	4.5–5.0	2.3–4.0	1.8
4–15	0.6–0.9	0.1–1.2	0.1
15–80+	0.2–0.3	0.2–0.3	0.1
Average	0.8–1.3	0.6–1.0	0.18–0.22

^a As defined by the World Bank (2003).

28.5 CONCLUSION

To effectively manage waterborne disease, it is necessary to consider the total burden of disease from all water-related exposure routes (drinking-water, contact with recreational water, the use of wastewater in agriculture, and contamination of other food items, e.g., shellfish). The Stockholm framework provides a tool for developing guidelines and standards to manage the disease burden from all water-related exposure routes. Framing health outcomes in terms of DALYs allows one to compare the health impacts associated with different diseases in a population, such as an infrequent case of cancer versus more frequent cases of mild diarrhoea, and thus enables priority setting to maximize health protection. Health risks should be put into the context of tolerable risk, which can be redefined as new technologies or other developments facilitate the reduction of health impacts from waterborne exposure routes or specific pathogens.

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29

Quantitative microbial risk assessment issues

G.B. McBride

29.1 INTRODUCTION

Epidemiological studies and surveillance activities are a vital part of region-wide and country-wide efforts to understand the human health risks associated with waterborne zoonoses and to set appropriate public policy (see chapter 10). Another approach is to use quantitative risk assessment (QRA). The essence of QRA lies in its four main steps:

- (1) hazard assessment;
- (2) exposure assessment;
- (3) dose–response analysis; and
- (4) risk characterization.

© World Health Organization (WHO). *Waterborne Zoonoses: Identification, Causes and Control*. Edited by J.A. Cotruvo, A. Dufour, G. Rees, J. Bartram, R. Carr, D.O. Cliver, G.F. Craun, R. Fayer, and V.P.J. Gannon. Published by IWA Publishing, London, UK. ISBN: 1 84339 058 2.

The concentration of zoonotic microorganisms (Step 1) and the extent of exposure (Step 2) vary between individuals, locations, and occasions. Simple calculations of average risks using average concentrations and exposures can therefore be seriously misleading. Accordingly, it is necessary to use random statistical sampling from the distributions of these variables to build up a risk profile.

In performing these calculations, QRA draws on information from epidemiological studies and surveillance activities (in selecting the pathogens of concern in Step 1; quantifying the degree of exposure in Step 2). It also draws on material available in the scientific literature (especially for Step 3). The risk characterization (Step 4) is useful in its own right, as a means of indicating important aspects of waterborne transmission of zoonoses. It may also be used to modify and refine epidemiological and surveillance efforts, thereby leading to more effective public policy and animal husbandry practices that lessen risks of waterborne transmission of zoonotic microorganisms.

This brief chapter gives an example of the application of QRA to waterborne zoonotic organisms (*Campylobacter*) and highlights some strengths and weaknesses of the approach. Details of the application methodology are not given, as they are well described in existing texts (Haas *et al.* 1999; Haas and Eisenberg 2001).

29.2 CAMPYLOBACTERIOSIS CASE-STUDY

The incidence of campylobacteriosis is of concern in New Zealand, with the surveillance system showing that it currently comprises over half the country's notifiable disease burden (see chapter 12). An epidemiological study by Eberhart-Phillips *et al.* (1997) has indicated that undercooked chicken is a major risk factor, but it has also identified other factors, including contact with animals and use of rainwater as a source of water at home. The study by Eberhart-Phillips *et al.* (1997) did not seek information on contact with recreational water, so the importance of that factor could not be assessed. Since that study, *Campylobacter* species have often been found in water samples at recreational sites. Given that it is a potentially waterborne disease and that farmed animals commonly have direct access to waterways, there has been interest in assessing the degree to which contact with recreational water may play a role in the transmission of *Campylobacter*.

This question is best addressed by a QRA approach, as has now been reported (McBride *et al.* 2002). The study by McBride *et al.* (2002) focused on infection, rather than illness, as its health outcome, for two reasons. First, avoiding infection also avoids illness, but the converse is not true — there can

be many passive infected carriers of this microorganism, whose shedding can cause infection *and* illness in others. Second, the available dose–response relationship for infection is more straightforward than the relationship for illness (as discussed below).

The main results are summarized in Table 29.1, which shows the percentile of time that risks reach a given case rate. This has been done by Monte Carlo simulations of exposure of 1000 people (each with a different degree of exposure) on each of 1000 occasions — a million calculations in all. Furthermore, two separate target populations were considered. In the first case, the *local population*, all 1000 attended the same beach on any given occasion, so on that occasion they were all exposed to the same (randomly selected) *Campylobacter* concentration; on another of the 1000 occasions, they were all exposed to another *Campylobacter* concentration; etc. In the second case, the *dispersed population*, all 1000 people attended a different beach on any given occasion, so on that day they were each exposed to a different *Campylobacter* concentration.

As a result, the risk profiles for the two populations are quite different, although the mean number of cases over the million exposures was about the same (about 40 500). For the local population, the risk is usually completely negligible, because the beach is uncontaminated for a majority of the time. However, when the beach is somewhat contaminated, substantial infection rates could occur if recreational activity was occurring. On the other hand, there is always some contamination at some beaches, so there is always some risk at some beaches, and so the dispersed population has a much flatter risk profile.

The results for the dispersed population have been used, along with the notified illness rate, estimates of under-reporting rate, and the proportion of passive carriers, to deduce that 4–5% of the actual number of *Campylobacter* infections could be the result of exposure to recreational fresh water (it is coincidental that the average case rates in Table 29.1 are also in this range).

At first sight, it may seem that this figure (4–5%) does not suggest an important transmission route, and the QRA results could be ignored. Two matters suggest otherwise. First, this result is for freshwater exposure only. It does not consider recreational exposure to estuarine and coastal waters or exposure via the consumption of raw shellfish (commonplace in the New Zealand setting, with its rich coastal resources). Second, water is an effective conveyer of microorganisms from one location to another. For example, infection in an animal herd towards the top of a watershed can be transmitted rapidly downstream to other herds, which may also become infected via contaminated water, further increasing the risk of waterborne transmission.

These results have been used in public policy, especially in the setting of new microbiological water quality guidelines for freshwater recreational areas, using

the moderate correlations observed between concentrations of *Campylobacter* and the much more easily assayed *E. coli* (Ministry for the Environment and Ministry of Health 2003).

Table 29.1. Two types of risk profiles (McBride *et al.* 2002)

Percentile ^a	Campylobacteriosis infection risk (per 1000 recreational events)	
	Local population (1000 people at the same beach each day) ^b	Dispersed population (1000 people at 1000 different beaches each day) ^c
Minimum	0	25
2.5th	0	29
5th	0	31
10th	0	33
15th	0	34
20th	0	36
25th	0	37
30th	0	38
35th	0	38
40th	0	39
45th	0	40
50th	0	41
55th	0	42
60th	1	43
65th	3	44
70th	9	44
75th	18	45
80th	26	46
85th	72	47
90th	131	49
95th	329	52
97.5th	435	54
Maximum	491	62

^a Percentage of time that the infection rate is up to the value shown in each row.

^b Each of the exposed “see” the same random pathogen concentration at any one time.

^c Each of the exposed “see” a different random pathogen concentration at any one time.

There are, of course, some uncertainties in this work, and these need to be recognized.

29.3 UNCERTAINTY IN QRA

QRA is designed to accommodate uncertainty and to quantify the consequences of that uncertainty. Yet it is itself uncertain! Consider the fundamental elements:

- (1) the choice of appropriate zoonotic pathogen(s);
- (2) the quantity of the pathogens deposited by animals;
- (3) their transport and inactivation over the landscape to water bodies;
- (4) the efficacy of water supply or wastewater treatment processes (e.g., waste stabilization ponds, stream riparian retirement);
- (5) the pathogen concentration in the water conveyed to humans — for drinking, for recreation, or indirectly following filtration by shellfish;
- (6) the degree of exposure (exposure duration and ingestion/inhalation rate during recreational exposure), or the amount of shellfish consumed;
- (7) a dose–response relationship showing probabilities of infection related to the received dose; and
- (8) calculation methods.

To a greater or lesser degree, there is uncertainty in all these items, many of which have been addressed elsewhere in this book and need no further elaboration here. Here we particularly address the last two issues.

29.3.1 Dose–response

Some waterborne zoonotic pathogens have been the subject of clinical trials, including *Salmonella* (multiple non-typhoid strains), *E. coli* (non-enterohaemorrhagic strains, except O111), *Campylobacter jejuni*, *Cryptosporidium parvum*, and *Giardia lamblia* (Teunis *et al.* 1996; Haas *et al.* 1999; Haas and Eisenberg 2001). Data from these trials are fitted to dose–response curves (generally a single-parameter exponential model or a two-parameter beta-Poisson model). Issues arising are as follows:

- Subjects in clinical trials are usually restricted to healthy adults, so the young, infirm, and immunocompromised are not represented.
- Trials typically administer few — if any — low doses (Rollins *et al.* 1999; Tribble *et al.* 1999). Consequently, there is considerable uncertainty in the dose–response relationship at low probabilities of infection or illness (Teunis and Havelaar 2000). Yet such doses are often typical for exposure to contaminated water and therefore crucial in the risk assessment calculations. For an example, see the beta-Poisson *Campylobacter jejuni* relationship on Figure 29.1 (from the beta-

Poisson model reported by Medema *et al.* 1996); only one dose lies below the calculated median infective dose.

- Trials are generally restricted to one strain of an organism. The infectivity of that strain may differ from that of other strains. For example, trials have been performed on different strains of the same organism, with substantially different infectivities being found (i.e., for *Cryptosporidium parvum* — Okhuysen *et al.* 1999; Teunis *et al.* 2002a, 2002b). Similarly, there are hints of the same for *Campylobacter jejuni* (Bacon *et al.* 1999; Stewart-Tull *et al.* 1999).
- Infectivity may also be affected by the manner in which the pathogen is stored and passaged in the laboratory.
- Dose–response curves for infection given dose are monotonic-increasing, whereas curves for illness given infection may not be (Teunis *et al.* 1999). Regarding the illness curves, examples can be found for three possible alternatives: an increase in the probability of illness with increasing dose (salmonellosis), a decrease with higher doses (campylobacteriosis), and a probability of illness (given infection) independent of the ingested dose (cryptosporidiosis). These alternatives may reflect different modes of interactions between pathogens and hosts. For example, a decreasing illness probability with dose may be found if higher doses elicit progressively stronger defence reactions in hosts, thereby preventing further damaging activities in those hosts (Teunis *et al.* 1999). Further dose–response studies would be necessary to clarify the strength of these findings. (As noted above, this is one of the reasons for making infection the endpoint of an analysis, rather than illness. The other reason is that avoiding infection also avoids illness, but the converse is not true.)
- Clinical trials have not been conducted for many zoonotic waterborne pathogens, so they completely lack dose–response data.

Ways to address these issues need to be found in order to improve QRA — and, in some cases, to even make it possible to perform it.

29.3.2 Calculation methods

While good advice is now available in texts (Haas *et al.* 1999; Fewtrell and Bartram 2001), some calculation issues remain to be addressed — or, at least, reinforced. These issues include the following:

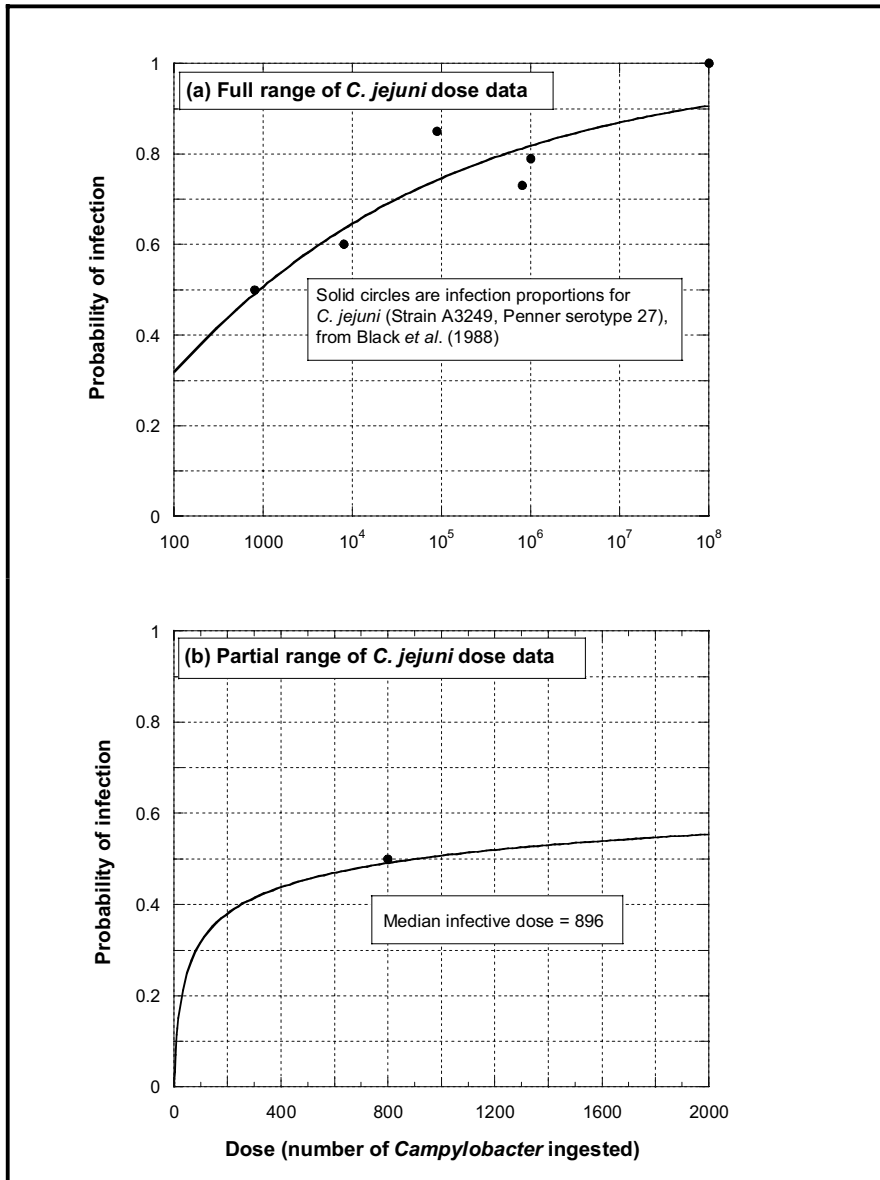


Figure 29.1. Dose–response curve for *Campylobacter jejuni* over full and partial range.

- Some data are known to be variable (e.g., pathogen concentrations in water). These are characterized by statistical distributions. To calculate risk, these distributions need to be combined with dose–response curves.
- Risk will be underestimated if that combining is effected merely by comparing the median infective dose with an average actual dose.
- Calculation of risk therefore does not result in a number, but in a *distribution* of numbers showing a risk profile (e.g., see Table 29.1).
- Combining distributions can, in some cases, be done using formal analytical methods. However, numerical methods are usually needed, such as Monte Carlo random sampling, for which commercial software is available. Care must be taken if any of the variables are correlated (Haas 1999).
- Statistical distributions cannot be directly fitted to most probable number data (e.g., for *Campylobacter*). These data are defined on a number system in which no two numbers have equal occurrence probabilities under random selection; some numbers are actually impossible. Instead, a “binning” procedure can be deployed, with a distribution being fitted to the bins (e.g., McBride *et al.* 2002).
- Concentration distributions can be multimodal, so selecting a unimodal distribution from the standard set available in most software will underestimate the occurrence probability of extreme values, leading to potentially serious underestimations of risk. In such cases, either mixture distributions or empirical distributions must be used.
- The target population must be defined. In addressing regional or national policy issues, the target population may be exposed at many sites. In that case, the calculation for any particular time of exposure should assign a different, random pathogen concentration to each exposed person. That being so, the risk profile will tend to be rather flat, because at least a few sites may be sufficiently contaminated at any one time to give rise to infection. On the other hand, if the interest is in a particular site, then all people at that site can be at risk.
- While the above reasoning calls for a number of people (e.g., 1000) being exposed at any one time, it can often be satisfactory to use just one exposed person at each time. This makes for rapid calculation. However, for very infective organisms (e.g., with a single-figure median infective dose), this strategy produces error. In an extreme case, consider a pathogen with a probability of infection given ingestion of a single particle of 0.34. If that one person is predicted to have ingested a particle, then that translates to about 340 predicted cases of infection per 1000 individuals; otherwise, there will be no cases. This is not tenable. What in fact will happen is that a few

of the 1000 people may become infected — many less than 340, but more than none at all.

- Presence/absence data are problematical for risk analyses. One must use “added zeros” distributions and expert elicitation of bounds on concentrations (McBride *et al.* 2002).
- Dynamic epidemiologically based risk assessment models may be used to take account of secondary (person-to-person) transmission, long-term and short-term immunity, and environmental population dynamics (Haas and Eisenberg 2001; Soller *et al.* 2003).
- Risk profiles are best understood by policy-makers as predicted cases of infection per unit of the exposed population (e.g., per 1000 people).

29.4 CONCLUSIONS

QRA is but one technique in overall risk analysis. It has the potential to be particularly useful, especially for scenario modelling — the “what if?” approach. For example, if the efficacy of installation of wastewater reticulation and treatment systems or of riparian retirement can be established, then quantitative risk models can be used to look at likely improvements to human health. Yet many gaps remain to be filled before QRA can be used with confidence to help in setting policy and managing use of water resources. The greatest deficiency appears to be the absence of dose–response data for many waterborne zoonotic pathogens. All this being so, the case for performing quality audits of waterborne risk assessment (Macgill *et al.* 2001) is well made.

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