

A REPORT FROM THE AMERICAN ACADEMY OF MICROBIOLOGY

# Clean Water



WHAT IS ACCEPTABLE MICROBIAL RISK?



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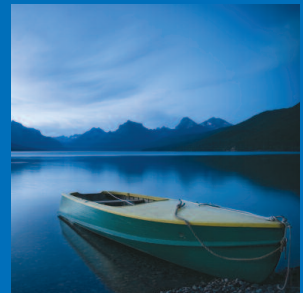
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BY MARK LECHEVALLIER AND MERRY BUCKLEY

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# I. Introduction



Access to clean water is essential for life. In recent decades, technology, civic progress, and an abundance of resources have enabled developed countries to cultivate high-quality water sources and distribution systems. As a result, people in these countries now enjoy lower infectious disease rates, higher hygiene standards, and a higher quality of life than has ever been witnessed in history.

It is a familiar scenario: an outbreak of gastrointestinal illness suddenly emerges in a community, and no one knows where it came from or how to stop it. At the start of an outbreak, only a few people are affected with the uncomfortable consequences: nausea, vomiting, cramping, and diarrhea. Sick people trickle into doctors' offices and clinics for help. Among them are elderly patients and small children, some of whom are admitted to the hospital. As the outbreak worsens, more and more people fall ill, and individuals who were weak or unwell before they became infected may develop life-threatening illnesses. Outbreaks like these can originate from a source that most people in the U.S. and other developed countries trust unquestioningly—drinking water.

Although drinking water quality in developed countries is high, a number of outbreaks of waterborne illness are still reported every year (Dziuban, et al., 2006). Worldwide, the statistics are even more alarming: two million people die every year from diarrheal illness, most of which can be attributed to waterborne pathogens (Pruss, et al., 2002; [http://www.who.int/water\\_sanitation\\_health/publications/facts2004/](http://www.who.int/water_sanitation_health/publications/facts2004/)). Even more alarming is the situation in the developing world, where access to clean water is far from guaranteed, and diarrheal illnesses claim roughly 2 million lives every year, 90% of them small children ([http://www.who.int/water\\_sanitation\\_health/](http://www.who.int/water_sanitation_health/)).

Today, scientists have a relatively new tool for addressing the problems of waterborne infectious disease: microbial risk assessment (MRA), a formal process for quantifying the health risks from pathogenic microorganisms. MRA is guided by a framework, which defines the activities necessary to obtain information required to develop a quantitative model for calculating health risks.

The American Academy of Microbiology convened a colloquium October 6-8, 2006, in Tucson, Arizona, to review the status of microbial risk assessment as it applies to waterborne disease. Experts from diverse fields—including microbiology, public health, engineering, epidemiology, medicine, and water science—discussed some of the controversial topics in microbial risk assessment, research subjects that could move the field forward, and the need for increased training and risk communication.

The colloquium elicited intense discussion as there is still need to solidify approaches to the microbial risk assessment of water. Numerical water

quality standards, for example, are useful in some circumstances, but they are sometimes misapplied or calculated using specious assumptions. The term "acceptable risk" is also controversial. "Acceptable risk" implies that injuries from waterborne illness are expected and fitting, and acceptable risk figures may be appropriately used to derive water quality standards in some instances. For a number of reasons, much of the data available on microbes in water is related to indicator organisms (microbes that denote the presence of fecal material or pathogens), but these organisms are not a substitute for counting the actual pathogen concentrations in water.

Another difficult point is sometimes reconciling the approaches between microbial risk assessment and epidemiological studies. The approaches, although potentially harmonious, often lack coordination. However, epidemiological studies can be extremely useful in identifying risks and every effort must be made to reconcile epidemiological and microbial risk determinations.

An accessible international database of pathogen occurrence in water would be extremely useful. Making data of this kind more widely available would inform microbial risk assessment and risk management and enable implementation of public health initiatives that could save lives.

Microbial risk assessment of water is an evolving field, and a great deal of novel research is needed to fill gaps in the understanding of human exposure to pathogens in water, to determine the current rate of waterborne illness, the dose-response relationships between pathogens and human health, and the role of waterborne opportunistic pathogens in human health.

Since the field of microbial risk assessment relies on the skill sets of professionals in many disciplines, education and research in microbial risk should be interdisciplinary and collaborative.

Finally, there is a need to effectively communicate microbial risk principles to consumers and the general public because a lack of information can have serious implications for communities. Risk managers and public health authorities need to make increased efforts to educate the public on everyday matters, like the need to change the filters in water purifiers and the need to upgrade and maintain water and wastewater treatment facilities.

For all the challenges that still exist to advancing the science and application of microbial risk assessment, the effort to do so will offer many benefits. A primary advantage of the iterative process is that it helps to identify data gaps and uncertainties, and it focuses limited research resources towards key parameters that will improve the understanding of risk. When applied correctly, microbial risk assessment can help guide water quality management decisions; identify sensitive subpopulations, spot critical pathogen control points, and aid in assessment of the adequacy of drinking water treatment barriers.

# II. Introduction to Microbial Risk Assessment



In outbreak situations, scientists and public health authorities have countless questions to address. Which water treatment option is best for preventing illness and death? Who are the most sensitive members of the population? How can we protect them? Where should efforts and resources be directed to prevent waterborne disease? What are the most dangerous pathogens found in water? How did they get there? How do we set standards for water quality and what is “safe water”?

All these questions can be addressed using microbial risk assessment—a formalized approach for identifying the risks arising from contact with pathogenic microorganisms, including certain bacteria, viruses, and microscopic eukaryotes. But microbial risk assessment is more than a tool for calculating risks. If applied correctly, microbial risk assessment can help guide management decisions, identify sensitive groups, spot critical pathogen control points, and aid in assessment of the adequacy of drinking water treatment barriers.

## WHAT IS RISK?

“Risk” means different things to different people, but the term can be boiled down to the sum of three considerations:

- What can go wrong?
- How likely are the various results?
- How bad are the possible results?

Hence, risk is the likelihood of identified hazards causing harm (great or small) in a specified time frame. In the context of microbial risk assessment, risk is the probability of an adverse outcome given a defined set of host, microbiological, and environmental factors.

With respect to environmental hazards like pathogenic microorganisms, toxic chemicals, and other materials that pose a threat to human health, exposure is another consideration in risk. The greater an individual’s exposure to a hazard, the greater the risk. Risk is a multi-faceted phenomenon, and although simplistic definitions or equations do not capture the full context of how individuals and risk assessment professionals view or evaluate risk, they do depict the basic concepts. A simple equation describes this relationship:

$$\text{Risk} = \text{Hazard} \times \text{Exposure}$$

There are three major components of microbial risk associated with water contact: the host (human), the microorganism, and the environ-

ment. Each of these factors is extremely complex. The characteristics of the human host, for example, vary widely from person to person, and some people are more susceptible to infectious diseases than others. A risk assessor must narrow down the characteristics of the host, microbe, and environment so that the risk assessment considers enough factors to be accurate, but not so many that the assessment is overly complicated.

In assessing the risk of disease that arises from contact with water, the immediate concern is separating the cases of interest (diseases that arise from contact with water) from illnesses that arise from other activities, such as person-to-person contact or from contact with infected animals. In this context, the disease burden associated with exposure to water is called “attributable risk.”

The characterization of microbial risk relies on knowledge of the duration and severity of the various possible outcomes. For example, a risk assessment must distinguish protracted, severe cases of disease from brief, mild ones. (This issue is thoroughly discussed by Rose and Grimes (2001) and in chapter 1 of the book *Water Quality—Guidelines, Standards, and Health: Assessment of Risk and Risk Management for Water-Related Infectious Disease* (2001).)

Ideally, microbial risk assessment should be a structured, integrative process that is thoroughly documented and based on sound science. It should be repeatable, transparent, flexible, relevant, and iterative. Good risk assessments make use of the best available evidence, clarify the impacts of any assumptions and any defaults used in the process, and include explicit analysis of uncertainties and the sensitivity of individual parameters and assumptions. Furthermore, risk managers (individuals charged with limiting risks to the public) should be involved in the formulation of the problem statements that guide risk assessments. In addition, in evaluating disease risks resulting from contact with water, assessors should consider accumulative risks. For example, an assessment should consider the risks resulting from exposure to all the pathogens that might be found in a glass of water, not just the risk due to a handful of select pathogens.

Finally, since individual choices about water use can cloud the situation, risk should be based on sound science and characterized at the population level, not the individual level. This allows assessors to account for the immune compromised segment of the population and for diseases arising from secondary transmission.

## WHY MICROBIAL RISK ASSESSMENT IS A VALUABLE TOOL

Any environmental assessment relies on imperfect information. Microbial risk assessment is no different. However, the microbial risk

assessment process presents a systematic framework to integrate highly diverse sources of information into a coherent process. Even with highly imperfect information, microbial risk assessments are a useful tool to identify the value of additional information and direct resources towards filling the most critical data gaps.

Although microbial risk assessment is considered as a process with specific frameworks and steps, the highly iterative nature of the process can be better described as a circle signifying no absolute beginning or end. The risk cycle signifies that one can enter the process at multiple points, and the circle emphasizes the need to reiterate the process. There is not necessarily a final answer; rather, there are multiple answers with each turn of the cycle. If the process is done well, and each stage is a learning process, microbial risks assessments are an efficient way of organizing, prioritizing, and refining the information.

The application of iterative microbial risk assessments for setting standards for water and food, as well as evaluating the impacts of risk management options and critical points in the water treatment process, allows the risk manager to develop a disciplined and reproducible approach for establishing risks and evaluating competing (e.g., microbe/microbe or microbe/chemical), accumulative, or even delayed risks.

The investment in developing sound microbial risk assessment will provide policy makers with sensitive tools for making public health decisions, evaluating cost/benefits, and avoiding unintended consequences. Although there are still many challenges to fully realizing all the benefits of the microbial risk assessment process, the ability to integrate information from diverse sources, leading to an enhanced understanding of factors that influence risk, provides the risk manager with insights and critical knowledge to potentially mitigate risk.

In addition, a risk model provides a platform for scenario analysis; that is, by changing the inputs, hypothetical situations can be examined for their potential effect on individual components and on the final risk outcome. Scenario analysis can also indicate the value of data that are lacking, and substitution of assumptions about the data gaps can indicate if better or more data would actually change the outputs of the assessment. Finally, the simple documentation and transparency (the clear statement of assumptions) of the process can facilitate communication among scientists, risk assessors, policy makers, regulatory authorities, water utility operators, and the public.

For all these reasons, microbial risk assessment, when conducted properly and iteratively, is a valuable tool.

#### WHO IS DOING MICROBIAL RISK ASSESSMENT?

Microbial risk assessments are conducted by the World Health Organization (WHO) for drinking water, waste water, and recreational water. The U.S. Environmental Protection Agency (EPA) also carries out risk assessments of drinking water and ambient waters to set regulatory standards. These assessments tend to show that pathogenic microorganisms pose a significant environmental hazard. Some water utilities also conduct microbial risk assessments as a means of evaluat-

### The Risk Cycle: An Iterative Process

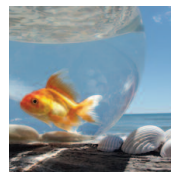


ing the adequacy of their treatment processes or to determine how to comply with water quality regulations.

In the U.S. government, an interagency working group has been assembled to develop federal microbial risk assessment guidance. The EPA Office of Water is developing a Microbiological Risk Assessment Protocol for water-based media that will have an accompanying Thesaurus of Terms and Definitions for microbial risk assessment applications (terms used by U.S. agencies, international agencies, and researchers). Currently, the EPA is working with the U.S. Department of Agriculture (USDA), the U.S. Food and Drug Administration (FDA), the U.S. Department of Defense (DOD), and the U.S. Department of Homeland Security (DHS) to establish interagency microbial risk assessment guidelines for food and water. The EPA Risk Assessment Forum has a goal of establishing agency-wide guidance for microbial risk assessments for air, water, solid waste, biosolids, genetically-modified microorganisms, and microbial pesticides. Independently, U.S. government agencies are conducting collaborative efforts to develop or refine general microbiological risk assessment tools, methods, and protocols under the umbrella of the Interagency Risk Assessment Consortium.

To help guide this process, the formation of an independent microbial risk assessment advisory board (based on the model of the National Advisory Committee on Microbiological Criteria in Foods) is recommended in order to encourage more consistent use of the best techniques for evaluating the problems of public health and water quality. Since a number of key experts are outside the U.S., consideration should be given to creating a board with international representation. The board could be composed of scientists from both industry and academia. Non-risk assessors should also be part of such an advisory board because the perspective of diverse stakeholders will be useful in formulating specific problems.

# III. The Current Microbial Risk Assessment Landscape



Microbial risk assessment of drinking water is a relatively new area of investigation, and there are many complex issues that still need to be addressed by scientific and regulatory agencies. Topics that require attention and dialog for those interested in risk assessment include:

- development and application of numerical water quality guidelines,
- definition of “acceptable risk,”
- identification of appropriate indicators of risk,
- harmonization of epidemiology and risk assessment,
- use of safety factors,
- model validation, and
- quality assurance and quality control.

At the end of this section, specific recommendations are presented for an international database on the occurrence of waterborne pathogens. Consolidating federal microbial risk assessment resources and efforts is also highly recommended.

## CURRENT LEVELS OF RISK FOR DRINKING WATER AND RECREATIONAL WATER

It is difficult to make broad statements about the current levels of risk associated with exposure to drinking water and recreational water, since these calculations depend in part on the available methods of specific microbe detection (which typically do not recover all waterborne microbes), human exposure profile, and on the definitions of health outcomes of concern. The development of reproducible methodologies and consistent definitions for use in microbial risk assessment are necessary to facilitate these determinations.

## NUMERICAL STANDARDS: ARE THEY USEFUL GUIDELINES?

Numerical standards, which set limits on either the number of organisms in a given volume of water, or on the number of illnesses per person per year in the exposed population, are useful and appropriate for guiding improvements in drinking water quality. For standards to be meaningful and enforceable, both scientifically and legally, they must have a certain level of confidence. However, the level of confidence in the data can be fraught with uncertainty, and outlining a sound rationale and clear explanation of the steps in the calculation is essential.

Managing risks associated with water exposure entails making trade-offs in resources, and reducing one risk often means increasing another. If resources are spent in order to meet a numerical water quality guideline, the benefits of making those changes need to be understood within the context of other public risks and the costs associated with reducing those risks. Hence, it is critical that the calculations and assumptions behind numerical guidelines be clearly put forth and understood by risk managers.

Although numerical standards are useful, they are not a panacea. One number can never be protective in all scenarios, for all pathogens, and for all segments of the population. For example, numerical standards are only protective for the routes of exposure that are accounted for in their calculation, and water standards that are based on the consumption of drinking water may be protective for other exposure scenarios, including the inhalation of aerosolized water, which can deposit waterborne microorganisms to the lungs. Again, understanding the calculations and parameters used in determining a standard is essential to the correct use of that standard.

In defining standards for water quality, the WHO and EPA aim for water quality targets that are protective of individuals experiencing all the “normal” life stages. These standards strive to be protective of children, pregnant women, and the elderly, as well as the population at large, but they may not necessarily be protective of highly sensitive subpopulations, e.g., HIV/AIDS patients or other immunocompromised individuals. The expectation is that members of highly sensitive groups will be advised by their health providers to take specific, additional precautions, such as boiling water or using water filters, to avoid waterborne illness. This arrangement is expedient, since treating water to a level that would be appropriate for these subpopulations could be extremely expensive. Still, some questions arise with this approach:

- Who is responsible for protecting sensitive individuals? Federal health agencies or medical practitioners?
- Some people misunderstand the instructions given for self-protection. How can public health authorities be certain that everyone is given ample opportunity to avoid illness?
- Does this approach still make sense when the proportion of immunocompromised becomes large?

It may be best to avoid differentiating “normal” from “abnormal” states. By computing the costs and benefits across multiple susceptible groups (immunocompromised vs. those with healthy immune systems), decision makers can balance the overall cost effectiveness of various alternatives without having to attempt the difficult process of differentiating between “normal” and “abnormal” immune states.



In places where resources and expertise are scarce, performance targets, and even specific technologies, may be a more appropriate way for policy makers to express water quality expectations than using numerical standards.

The EPA considers one infection per 10,000 individuals in a given year as a reasonable guideline for potable drinking water. This number was derived in 1987 by determining the waterborne disease burden Americans already tolerated: the total number of reported cases of waterborne illness per year (then estimated to be 25,000) divided by the U.S. population (250,000,000 at the time) (Bennett et al., 1987).

## FOR STANDARDS TO BE MEANINGFUL AND ENFORCEABLE, BOTH SCIENTIFICALLY AND LEGALLY, THEY MUST HAVE A CERTAIN LEVEL OF CONFIDENCE.

However, the exact level of waterborne illness (endemic) is not known, and the level of infection not resulting in clinical illness (subclinical) is even less well defined. Because of these uncertainties, there is some controversy about the details of the EPA's calculations, and, therefore, about the applicability and usefulness of the 1/10,000 guideline for protecting public health.

For example, two recent exercises to calculate the current level of waterborne illness resulted in estimates of illness that range between 4 million and 33 million cases per year (Colford et al., 2006, Messner et al., 2006)—rates that roughly translate to 1/10 to 1/100 illnesses per year. Therefore, the estimates of the current landscape range between a 100- and a 1,000-fold higher than the stated guideline.

Moreover, the 1/10,000 guideline was developed without substantial consideration of the societal and public health conditions, risk perception in the community, or the resources of the society. In contrast, developing and implementing a series of interim goals that are relevant to the specific setting may be preferable to the single figure approach used by the EPA. Alternatively, focusing on a more descriptive endpoint (a measure of injury) rather than on the number of infections may reveal the true problems associated with poor water quality. The WHO approach, in which disability adjusted life years (DALYs represent the number of days that are lost due to sickness or death) quantify the risks from waterborne infection, may be more advantageous.

### WHAT IS A USEFUL GUIDELINE?

In designating a numerical standard, it is best to strike a balance between equity and economic efficiency. Equitable standards are worthless if society cannot afford to meet them. The quality adjusted life year (QALY), which is calculated based on the health of individuals (where 1 is perfect health and 0 is death) measures both the quality and quantity

of life lost to an adverse event. Thus the QALY could be a useful metric for measuring benefits to human health.

However, numerical standards should account for the possibility that multiple routes of exposure can play a role in disease rates. If water exposure accounts for only a small fraction of the total burden of illness from a particular pathogen, then it may not be worthwhile to set or enforce a strict water standard for that pathogen. In this case a dynamic systems approach is required, where the interactions of different routes of exposure are considered. Considering these interactions is important, especially in developing countries, where poor access to

hygiene and limited disease control programs result in high rates of infectious disease (although these factors can also apply in some cases to developed nations). An outbreak of norovirus, for example, can be initiated by water or food exposure, but contaminated surfaces soon become the dominant route of exposure. It is critical, therefore, that low cost interventions be developed that can be easily implemented. Disinfection of drinking water, collection and treatment of human and animal waste, and hand washing have been hailed as efficacious interventions that have dramatically reduced the burden of waterborne disease.

### DETERMINING AN ASSESSMENT ENDPOINT

During the planning stage, microbial risk assessors must identify the adverse phenomenon they hope to prevent. This outcome, called the "assessment endpoint," is a defining feature of any microbial risk assessment. Assessment endpoints can be organism- or disease-specific (e.g., *Giardia* versus giardiasis) or they can be syndromic, like acute gastroenteritis illness (AGI), which can result from an infection from any number of waterborne pathogens.

Risk assessors should consider many different assessment endpoints when planning an assessment, including:

- infection,
- acute illness (which may include respiratory illnesses associated with aerosol exposure or ear infections resulting from use of recreational waters),
- chronic illnesses and/or sequelae, and
- death.

# Determinants of Acceptable Risk



Acceptable risk is completely dependent on the context of the situation, including the affected population, preceding events, the extent to which exposure is voluntary, time, and, importantly, location.

## THE PEOPLE AFFECTED

What is “acceptable” is determined, in large part, by the consumers experiencing the risk. In addition, cultural factors and aesthetics can also play a role in what a group deems acceptable.

## PREVIOUS EVENTS

Public acceptability is frequently event-driven, and disasters often precipitate regulatory change. For example, communities across the country became concerned with the quality of their drinking water and pressured public officials for more stringent standards in the wake of the outbreak of cryptosporidiosis in Milwaukee in 1993. Although crisis-driven risk perception is common, it is not particularly objective, and regulatory agencies should attempt to replace it with more scientific assessment processes. Even still, for many communities the perception of risk is often as important as the reality of risk.

## VOLUNTARY RISKS VS. INVOLUNTARY RISKS

The degree to which individuals feel that they can control their exposure to risk is another critical component in how a community perceives that risk and defines acceptability. In general, individuals are willing to accept greater risks when they can control their risk exposure. For example, in the U.S., the public [implicitly] accepts much higher health risks from swimming in recreational water, which is voluntary, than from drinking tap water, which is more or less obligatory.

Involuntary risk levels that susceptible individuals knowingly endure can serve as benchmarks for determining an equitable levels of risk for the rest of the community.

## TEMPORAL FACTORS

Acceptable risk is not static. As a community reduces waterborne risks and other similar types of risks, their acceptance of risk can also be diminished. For example, a town that once perceived their untreated drinking water as “acceptable” will probably reject the same water once hygiene standards and public health efforts have reduce the rate of disease from other sources. Individual judgments about acceptable risk can also change over time; the risks a young person will tolerate may be very different from the risks one might take later in life.

## LOCATION, LOCATION, LOCATION

Acceptable risk is largely dependent on location. Specifically, a community sees new risks in relation to existing risks, and existing risks can vary from place to place. Individuals are usually only willing to accept risks that are similar in magnitude to the risks or circumstances they already face. This might imply that local risk perception determines acceptable risk, but this would be true only if the local population had a clear understanding of the risk. Since often this is not the case, acceptable risk is often determined by state and federal regulations.

## COST

Cost-benefit analysis evaluates the trade-offs involved in implementing a drinking water improvement technique. The goal is to express the value of an intervention in terms of how much it costs versus how many lives are saved or cases of illness prevented.

Willingness to pay is another factor in acceptable risk. In many developing countries, people will pay a large proportion of their income for water that is often (and even knowingly) contaminated. The poor may pay more for water than wealthier citizens of the same country. In contrast, citizens of developed countries are often unwilling to commit even a small percentage of their income to clean water either because they do not perceive unclean water as a personal threat or they feel that they are not benefited by community supplied water.

Concerns can arise when acceptable water quality standards from one country are applied, completely out of context, in another country. Considering the supporting framework of existing risks, cost-benefit trade-offs, and willingness to pay, acceptable standards derived for developed countries are rarely a good fit in the developing world, and vice versa. Acceptable risk standards formulated in the developed world can be considered unattainable and irrelevant, and may misdirect scarce resources away from more significant public health problems in developing. For example, concerns about forming disinfection byproducts may have played a role in the reluctance to chlorinate South American drinking water during the cholera outbreak in the 1990s.

However, assigning lower standards for less developed agricultural countries leads not only to greater risks for the citizens of those countries, but can also lead to unforeseen risks for produce consumers in developed countries. Note that World Trade Organization Sanitary and Phytosanitary Agreement acknowledges that member countries have the right to determine their own appropriate level of protection, but creates the obligation that a member's food safety standards be based on an assessment of risk.

Assessment endpoints like these can be translated into composite measures of injury, like DALYs or QALYs (which, respectively, represent days of life lost due to disability or death and the quality of life lost to illness). Although knowledge about infection rates is important to understanding disease transmissibility, it may be advantageous to use composite measures (like the QALY or DALY) to represent a more comprehensive measure of adverse effects than alternatives such as disease prevalence or mortality rate.

The appropriate assessment endpoint for a particular risk assessment is dictated by:

- **The nature of the pathogen.** Risk assessments usually focus on the most significant problem caused by a pathogen, which might be either the most severe condition or the most common endpoint.
- **The population of concern.** A risk assessment may focus on the general public or on a particularly susceptible group, like the elderly.
- **Other specific objectives of the microbial risk assessment.** Assessors may be interested in tracking asymptomatic infections, for example, so that they can understand how widely a population has been exposed.

## THE CONCEPT OF “ACCEPTABLE” RISK

Acceptable risk can be defined as the level of risk that is protective of public health for a population considering cost, feasibility, and other considerations. Acceptable risk figures may be used to derive water quality standards or other goals. Ideally, these standards should be protective of health goals, understandable, tolerated by the public, scientifically defensible, implementable, and roughly equal to the other risks faced by members of the community. In addition, treatment and analytical technologies must exist to make achieving the goal feasible. Although an acceptable risk level can be difficult to identify, it is often necessary so that a management goal can be defined.

### Alternatives to the word “acceptable”

The word “acceptable” is burdened with troubling connotations. Use of the term “acceptable risk” could imply that health and life are fairly exchanged for affordable water. Other terms to convey anticipated risks may be preferable to “acceptable” in certain circumstances. “Achievable risk” is a risk level that can be attained, given the current circumstances. This term may be used in reference to involuntary situations in which a consumer has no choice but to accept the risk.

The WHO recommends use of the word “tolerable” with respect to the risks that can be borne by a particular community. When using the term “tolerable risk,” the WHO prefers to place emphasis on incremental improvement and encouraging progress rather than surrender in the face of unattainable standards.

### Recommendations for determining an acceptable risk estimate

Context is everything in acceptable risk, so determining an appropriate number relies heavily on the people at risk (also called

stakeholders), as well as the location, duration, and circumstances in question. Risk managers should minimize social inequities by paying attention to subgroups within the population and to the distribution of risk and benefits. It is not always possible to protect exceptional populations via customary means, but the process of setting water quality standards should strive to include responsibility for developing and implementing special methods to protect sensitive subpopulations.

Risk communication is another critical factor as it may not be reasonable to assume that the public understands the risks they confront in drinking water. Cost-benefit analysis is a tool for determining which expenditures on water quality development will result in the greatest health gain per unit of investment. No risk is acceptable if options exist that can reduce that risk at a reasonable price.

Acceptable risk figures should reflect actual health outcomes, not simply infection rates. Considering disease severity and using DALYs as a measure of injury may shift the emphasis of assessments away from waterborne parasites like *Cryptosporidium*, which causes severe but infrequent infections, and towards waterborne viruses, some of which may cause less severe illnesses but are much more common and more influential on human health. Incorporating health burden in acceptability calculations will identify the microorganisms that result in the greatest burden to a community and allow public health authorities to target interventions to specifically target these risks.

Acceptable risk values derived for the developed world typically do not work in developing countries, where the responsibility for clean water is often considered to belong to the consumer. External aide agencies may not have the luxury of contemplating acceptable risk, but instead find themselves in the unenviable position of setting health goals that attempt to reduce existing levels of disease until there is a greater capacity to sustain public water and health infrastructure. For these countries it is important to incrementally improve all measures of sanitation together—in other words, improving drinking water quality alone will not have nearly the benefit as coordinated improvements in waste treatment, personal hygiene, and other sanitation practices.

## METHODOLOGICAL CONSTRAINTS

### MICROBIOLOGICAL DATA

Indicator organisms, which include specific bacterial species such as *Escherichia coli*, and broadly defined classes of organisms like “fecal coliforms” or “total coliforms,” have traditionally played a significant role in evaluating the performance of water treatment processes. The occurrence of indicator organisms is used to infer the potential presence of fecal contamination and the potential for enteric pathogens.

Although most of the available microbiological data from drinking water pertain to indicator organisms, these results are not useful for quantitative risk assessments of drinking water. Indicator organisms may indicate the adequacy of treatment but they do not have a direct relationship to the risk

of illness. Importantly, indicator bacteria are not adequate for some pathogens, including viruses or protozoan cysts, because the bacteria are more easily removed by treatment and disinfection. For recreational waters, the concentration of microbial indicators can fluctuate substantially over short periods due to changes in wind direction, tide, rainfall, sun exposure, and time of day. For these reasons, there is a movement under way to measure pathogen numbers in specific scenarios.

Testing for the presence of indicator organisms can be slow and the results are available too late to avoid exposure and subsequent public health risks. For this reason, analysis of treatment process controls, implementation of multiple barriers of treatment, and specific response protocols can anticipate or detect events and prevent problems better than analyzing microbial water quality as it leaves the plant.

For microbial risk assessments, measurement of index pathogen populations can better extrapolate risk. Index pathogens are specific microbial strains where the relationship between exposure (number of pathogens ingested) and risk of infection has been characterized. Monitoring for index pathogens will become more practical when the cost, sensitivity, specificity, ease of use, and the speed of analysis are improved.

Although fecal indicator organisms are still used to monitor recreational water quality in the U.S., regulators have reduced their reliance on indicator organisms for determining water treatment requirements in favor of using treatment techniques based on marker pathogens.

### Other Water Quality Indicators

Other indicators exist that do not require the enumeration of microbes to infer water quality. They include:

- Rainfall measurements
- Treatment plant turbidity
- Distribution system main breaks
- Loss of a disinfectant residual
- Reduction or loss of water pressure
- Changes in the taste, odor, or color of the water

Although these indicators may not have direct linkages to public health outcomes, they can be used in a qualitative manner to indicate relative changes in water quality. In the United Kingdom, for example, quantitative and qualitative indicators are used to assign color-coded safety warnings to recreational waters.

### THE ROLE OF EPIDEMIOLOGY IN ASSESSING RISK

Controversy sometimes exists on whether microbial risk assessment or epidemiology is more useful for protecting public health, especially related to water. The simple answer to this question is “both,” since the two disciplines need to be integrated to effectively address problems



related to drinking water. Epidemiology and microbial risk assessment are complementary subjects; epidemiology focuses on identifying health outcomes, whereas microbial risk assessment is a useful predictive tool for detailed modeling of the possible ranges or distributions of the risk for a certain set of factors.

Microbial risk assessment needs to broaden the use of available epidemiologic data. Numerous types of data are available from epidemiologic studies (including published cohort studies, unpublished outbreak reports, serologic surveys, and disease surveillance systems). Studies and risk assessment exercises should include a multidisciplinary team of microbiologists, risk assessors, and epidemiologists to facilitate the integration of epidemiologic and microbial data into risk assessments.

Epidemiology can also be useful for determining the relative risks attributable to drinking and recreational water, detecting disease trends, assessing the contributions of individual pathogens in the overall burden of disease, and measuring the efficacy of interventions. Epidemiological information from outbreak investigations may be useful in microbial risk assessments, but outbreak data often have limitations in determining low-level or endemic cases of illness related to water. Therefore there will be a continued need for epidemiological case control or cohort human trial studies.

Because the level of concern for risk in drinking water is at very low levels (1/10,000 infections per year) there are practical difficulties in trying to validate or compare microbial risk assessments using epidemiological studies. Still, there is a need to provide such linkages. Studies are needed to integrate outbreak data to better estimate microbial infectivity under real-world conditions; and to evaluate infectivity and dose response for pathogens too dangerous for human challenge studies.

### MICROBIAL RISKS IN FOOD

The overall approach to food risk and safety is very different from the approach used for drinking water. In the U.S., food safety goals are pathogen-specific, aimed at decreasing the incidence of diseases caused by particular pathogens (although food-specific management strategies are sometimes implemented). Microbial food safety goals for several pathogens (including *E. coli* O157:H7, and *Salmonella*



*enteritidis*, for example) are expressed as population-based annual incidence targets. Performance is measured through the FoodNet surveillance system, but there are no specific linkages to evaluate the effectiveness of food safety measures in terms of health outcomes.

Despite this advanced approach to food-based risk assessment and the fact that many risk assessments have been undertaken specific to a given combination of pathogens and foods, none have been used to establish a regulatory limit of a pathogen.

Acceptable practice for microbial safety in foods varies by food and by the manner in which it is processed. Processed, ready-to-eat foods are held to “zero tolerance” standards, and should contain no detectable pathogens. Fresh produce is presumed to be ready-to-eat and should, theoretically, adhere to the same high standards as processed foods. Most raw meat, fish, shellfish, eggs, and poultry are allowed to have detectable pathogens (at very low levels), even though they are sometimes eaten raw. Only *E. coli* O157:H7 is classified as an adulterant in cut-up beef.

### THE USE OF SAFETY FACTORS IN MICROBIAL RISK MANAGEMENT

Safety factors are adjustments or multipliers that are used to either 1) increase the exposure estimate or 2) decrease the proposed “safe” exposure value determined in a risk assessment in order to compensate for uncertainty. One way to account for uncertainty would be for microbial risk assessors to incorporate safety factors in their work to ensure that consumers are not exposed to excessive risk. However, safety factors bias the final assessments toward overprotection and prevent managers from using risk assessments to perform meaningful cost-benefit analyses.

In general, safety factors should be avoided. It is more appropriate and scientifically defensible to deal with uncertainty explicitly than to assign arbitrary safety factors for susceptible populations, exposure uncertainty, etc. Explicitly accounting for uncertainty will lead to a wider range of risk estimates, but it is a more authentic representation of the data. For example, probabilistic distributions of risk may be used to express the results of an assessment. Therefore it is recommended that risk assessors embrace uncertainty, quantify the degree of uncertainty,

and seek to define variables in terms of either increasing or decreasing certainty. In the end it is up to the risk manager, once the risk assessment has resulted in as detailed an analysis as possible, to determine if additional safety factors are warranted. Safety factors then become part of a policy decision—and separate from a risk analysis.

### VALIDATING MICROBIAL RISK ASSESSMENT MODELS

Microbial risk assessment models should be validated to ensure that the models accurately represent reality and to facilitate the amendment of inaccurate assumptions. To accomplish this, models and model components should be compared against independent experimental and empirical data when they are available; outbreak data would be particularly useful in this regard. Also, data collected before and after implementing interventions to limit waterborne illness can be used to verify that the risk assessment model predicts the measured outcome.

### QUALITY ASSURANCE AND QUALITY CONTROL IN MICROBIAL RISK ASSESSMENT

Quality assurance (the activities involving planning, implementation, documentation and reporting) and quality control (activities that measure the attributes and performance of a process against defined standards), seek to ensure that the data are of the type and quality needed.

Quality assurance and quality control activities should include:

- Checks on data input to ensure accuracy,
- Data quality audits,
- Computer code validation,
- Articulating all assumptions in the risk assessment,
- Ensuring model transparency and revealing which data were used and which were excluded—and why,
- Peer review,



- Plausibility assessment, and
- Error magnitude estimates.

There is a need to develop consensus documents on standards, methodologies, and quality assurance requirements for conducting microbial risk assessments.

### RECOMMENDATION FOR AN INTERNATIONAL DATABASE ON WATERBORNE PATHOGENS

There is a clear need for an international database of pathogen occurrence in drinking water and ambient waters that can be readily accessed by interested users. Making data of this kind more widely available would inform microbial risk assessment and risk management and enable the implementation of public health initiatives that can prevent illnesses and save lives. Historical data, in particular, can help scientists identify and manage abnormal events.

The quality and form of the data included in a database of waterborne pathogens would need to be validated through well-defined and specific criteria. Also, data should be quantitative and include determinations of pathogen infectivity or culturability as well as pathogen counts conducted using molecular, nucleic acid based techniques. The relationships of pathogen concentrations measured by these different analytical methods would need to be expressed. Inclusion of pathogen virulence data or other information on properties that contribute to adverse effects on hosts is recommended.

The waterborne pathogens database must include information about variability and uncertainty in the included data, particularly information regarding spatiotemporal variability and the effects of extreme events. The database should be updated continually as new data are obtained. Decisions would have to be made about the funding of such an effort, but it can be argued that agencies that have an interest in microbial risk assessments (e.g., WHO, EPA, FDA, USDA, etc.) would greatly benefit

from such an effort and should be encouraged to develop collaborative arrangements to adequately fund the effort.

A great deal of public health data gathered using public funds are locked away and unavailable to risk assessors studying waterborne illness. All data sets financed by public money should be "protected" for use by the involved investigators for a period of time (possibly two to three years), then made publicly available. It is increasingly difficult to uncover health statistics, but it is in the public interest to make them broadly accessible to the scientific community. For all these data sets it would be important to insure the data quality was adequate in the data bases, which would place an additional burden on either investigators or the federal institutions sponsoring the studies.

### RECOMMENDATIONS FOR ENVIRONMENTAL AGENCIES

Currently, microbial risk assessment in the federal agencies is scattered and inharmonious and there are various types of scientific expertise that operate relatively independently of the program offices that develop regulations and need access to risk assessment. Developing an umbrella program that links together and harmonizes the various individuals and units of the federal government that carry out microbial risk-related work (as well as those units that can contribute data) could substantially increase the effectiveness of federal waterborne disease projects. There are already some nascent efforts in this area that include EPA, FDA, USDA, DOD, DHS, and CDC on an interagency Microbiological Risk Assessment Guidance working group, EPA Risk Assessment Forum Microbiological Risk Assessment workgroup. However, much greater coordination is needed to build on these initial efforts and to bring other organizations, including international agencies (such as WHO) into the process.

### RESEARCH NEEDS

Microbial risk assessment is a burgeoning discipline, and like any emerging field of study, there are numerous gaps in the understanding

of microbial risk that must be bridged with innovative research. In addition to the research needs touched on in the previous section (Microbial Risk Assessment: The Current Landscape), more work is needed to characterize human exposure to microorganisms in drinking and recreational water, determine the baseline burden of illness, investigate dose-response relationships, and explore the role of waterborne opportunistic pathogens in risk.

## EXPOSURE

Two intertwined factors exist with respect to exposure in microbial risk assessment: measuring a population's exposure to water, and appropriately characterizing the exposure in risk assessments.

Researchers are finding that it is the microbial quality of water in people's homes at the point of exposure, not the quality of water in wells or at water distribution facilities, which determines health outcomes. In one illustration of the importance of monitoring at the point of exposure, researchers working in West Africa failed to find a link between water quality in wells and health outcomes, but the correlation between the quality of water in containers in the subjects' homes and health outcomes was strong (Molbak et al. 1989). A recent summary of waterborne outbreaks in the U.S. revealed that the majority of illnesses were associated with problems in the premise plumbing and not in the utility network (Liang et al. 2006). Although the importance of monitoring close to the point of exposure is becoming increasingly clear, research is only beginning in this vein and more monitoring is needed.

Water "abuse" represents another poorly understood facet of pathogen exposure that could be addressed by more thorough monitoring at the point of exposure. Consumers have been known to store

impact of increased consumption if more data were available. Standardized methods for collecting consumption data are needed.

It is important to account for system variability that can lead to changes in exposure and microbial risk because short periods of exposure to high pathogens levels can result in greater risk. The characteristics of the source water, treatment failures, treatment sensitivity to environmental conditions, the integrity of the distribution system, and human behavior can all introduce variations into a risk assessment. There is a need for more data and analytical techniques that can inform microbial risk assessments about such variations—especially for variations in water quality in drinking water distribution systems.

There is a pronounced need for improved monitoring designs that can capture spatial and temporal variability in pathogen populations. EPA is evaluating the use of molecular methods of detection and quantification of various fecal indicators, especially for use in recreational water monitoring, to provide rapid beach water quality alerts when criteria are not met. The response time for this methodology is ~2-4 hours of analysis time. This approach could also have applications for drinking water distribution systems but it will require development of less expensive technologies that can be more widely and rapidly deployed to quantify environmental pathogens. For instance, event samplers could take water samples during rain storms, sewer overflows, or in water treatment plants during periods of high turbidity.

The possible impact of reclaimed water use on human health has limited the application of reclaimed water in certain settings, but these putative risks have yet to be thoroughly explored. The pathogens of concern and possible mechanisms of exposure to reclaimed water (including direct inhalation, inhalation of dust treated with reclaimed

## IN THE U.S., INTEGRATED SURVEILLANCE AND REPORTING OF LARGE AND SMALL OUTBREAKS OF WATERBORNE DISEASE IS NEEDED IN ORDER TO GET A GOOD UNDERSTANDING OF WATERBORNE DISEASE BURDEN.

water in jugs or use the same container repeatedly—activities that can cause the stored water to become contaminated by enteric pathogens due to poor handling, and the contamination may persist if containers are repeatedly used without adequate cleaning.

Microbial risk assessment faces a deficiency in water consumption data, including information about consumption of water other than drinking (i.e., recreation). Also, studies have suggested that as people age they drink more water, but quantitative information on this phenomenon is lacking. Microbial risk assessment could help identify the

water, etc.) need to be studied and understood in order to enhance decisions about effectively utilizing this resource.

The role of immunity in determining the response to exposure to waterborne pathogens is another area that needs further research. For example, it is not known whether immunity to less virulent strains of the same organism provides protection to more virulent strains or whether repeated exposures to a pathogen increase the incidence of autoimmune disorders. Indeed, there are examples of waterborne pathogens where prior exposure to less virulent strains increases the host resistance to subsequent exposures and examples where immunity results in a more



# Considerations for Dose-Response Studies

## ETHICAL ISSUES

- Risk versus benefits.
- Immunological status of test population.

## CHARACTERIZING THE PATHOGEN

- Virulence factors. (Identify the virulence factors and determine and how to measure them.)
- Polymorphism of virulence factors based on strain or isolate differences.

## CHARACTERIZING THE HOST POPULATION

- Age.
- Ethnic group/race.
- Sex.
- Health status. (Screen for other diseases using physical exams, blood tests, and other laboratory testing.)
- Markers of genetic susceptibility and resistance (genotype and phenotype).
- Blood type.
- Haplotype.
- Immune status:
  - Characterize innate immune factors.
  - CD4 counts (a measure of immune vigor).
  - T-cell functional analysis (in vitro, skin test. etc.).
- Evidence of prior exposure to target organisms:
  - Identify pre-existing serum antibodies to the target pathogen.
  - Enumerate T-cells and B-cells and determine their functions.

## PREPARATION AND DELIVERY OF DOSE

- Safety-testing of inoculum.
- Dosage measurement:
  - Viable dose: determine the percent of administered pathogens that are viable.
  - The distribution of microbes in a sample: homogeneous or heterogeneous distribution. Dispersed pathogens vs. pathogens within aggregates.
  - Spatial/temporal aspects of the dose: delivered in a bolus or throughout a day.
  - Quantitation: presence/absence tests, coefficient of variation, replicate trials and replicate tubes coefficient of variation, replicate trials and replicate tubes.
- Genotype of inoculum.
- Vehicle of delivery (gelatin capsule, glass of water, sodium bicarbonate before and after).
- Digestive state of host (nothing by mouth, food restrictions, dose with or without food).

## STUDY DESIGN

- Number of subjects.
- Number of doses.
- Range of doses.
- Number of subjects per dose.

## MEASURING HOST RESPONSE

- Screening for confounding factors (infections from other pathogens, etc.).
- Symptoms (type, self-reported vs. measured, severity indices).
  - Diarrhea (presence or absence, number and consistency of stools, weight to volume ratio).
  - Vomiting (presence/absence, number).
  - Other gastrointestinal symptoms.
  - Systemic symptoms.
  - Pathogen and/or toxin excretion.
  - Duration of excretion.
  - Titer of excretion over time.
- Detection of pathogen in biological specimens (sensitivity and specificity of assay, reproducibility, quantitation methods, genotyping organism post-passage).
- Sero-response (presence of serum antibody).
- Peripheral Blood Mononuclear Cells.
- Salivary antibody response (immunoglobulins A and G).
- Up regulation and down regulation of specific genes/proteins (using microarrays).
- Frequency and length of follow-up.
- Host diet diary and the impact of diet on gastrointestinal flora, as well as other exposures before challenge and during follow-up period.





severe illness. The critical task for microbial risk assessments is to understand and apply these differences when appropriate.

#### **DETERMINING THE BASELINE RISK OF ILLNESS**

To determine the impact of a water quality intervention on the health of a community, it is important to know the baseline cases of endemic waterborne illness under normal circumstances. Although the disease surveillance system in the U.S. does not capture waterborne illness very well, experts estimate that between five and 14 million cases of gastrointestinal illness per year result from water exposure (Colford et al., 2006). Other studies attribute roughly 10% of all gastrointestinal illness in this country to water and an additional 30-40% to food (see the special issue of *Journal Water and Health* Volume 04, Supplement 2).

Endemic rates of waterborne illness can be estimated using two approaches: an epidemiological approach in which the fraction of all illnesses are attributed to drinking water, or by microbial risk assessment based on exposure to key groups of waterborne pathogens. There are advantages and difficulties associated with either approach. When using the epidemiological approach, it is important to note that as water utilities introduce changes in treatment or operations, exposure to waterborne pathogens changes as well, which can confound study findings. Also, the definitions of various gastrointestinal illnesses have changed over the last 20 years, resulting in differences in epidemiological estimates. Finally, epidemiological surveillance is costly and the results from a single system may not be readily applicable to all water systems.

In the U.S., integrated surveillance and reporting of large and small outbreaks of waterborne disease is needed in order to get a good understanding of waterborne disease burden. However, there are political obstacles to developing this type of program, since no single agency possesses the federal mandate necessary to make it happen. Data collection could be improved and made more useful by initiating community-based data collection systems. Such collection systems monitor sentinel parameters (e.g., emergency room visits, anti-diarrheal drug sales, school absences, nursing home illnesses) that can produce a

wealth of cohesive information to provide estimates of illness, sources, and casual linkages. Alternatively, it may be possible to devise a system to provide incentives for physicians who test and report results for significant public health pathogens.

Calculating endemic baseline estimates from risk assessment offers certain advantages. The dose-response relationships for several important viruses and for *Cryptosporidium* are fairly well understood. The challenge, however, is accurate estimates of exposure. Exposure assessment should be used to reveal what, exactly, people are exposed to over time, since a “snapshot” in time does not accurately depict long term exposure. Determining exposure to sensitive subpopulations is particularly important for accurate microbial risk assessments. Human subpopulations (such as infants, the elderly, and the immunocompromised) are not homogeneous, so extrapolating reliable estimates of subpopulation illness rates from exposure data can be difficult. Also, the consequence of infection can differ for sensitive subpopulations. Asthma patients, for example, are no more liable to contract waterborne infections than the general population, but they can suffer worse consequences if they do become infected.

#### **DOSE-RESPONSE STUDIES**

Pathogen dose-response studies determine the relationship between the number of pathogens administered to an individual and the disease elicited by such a dose. In other words, dose-response studies identify the likelihood of infection associated with different doses of microorganisms, the proportion of infected people who remain asymptomatic, and the proportions who experience mild, moderate or severe illness. Microbial risk assessment relies on dose-response data to make the leap from the number of organisms in a glass of water to an estimate of the risks that people face from consuming the water.

Although there are good dose-response data for some pathogens (notably *Cryptosporidium* and some viruses), there are no reliable dose-response data available for many other waterborne pathogens. A great deal of research lies ahead in this area. In addition, variability among

various pathogen strains can be substantial, but few data are available. Variability in infective dose data among just three strains of *Cryptosporidium* has been found to be considerable (Messner et al. 2001).

Dose-response studies can be extremely challenging to perform, and there are a number of complex factors to manage. In characterizing the host population, for example, it is important to evaluate the immune status of the group by gathering evidence about prior exposure to the target pathogens. Verifying the dosage and viability of pathogens administered to the subjects in dose-response studies is another critical point that is sometimes missed. The genetic and immunologic heterogeneity of the human population with respect to pathogen response is important and requires further study. It may be possible to develop a dose response model with co-variables for sets of genetic markers for susceptibility to a certain pathogens, and with information on the distribution of markers in the subpopulations, a risk model could be developed at the population level.

Generally, the infectivity of human pathogens for humans is high; in many cases it is possible to show a theoretical risk of infection from a single infectious unit. Illness, however, is a different issue altogether, and is primarily dependent on host status and variability among pathogen strains. In addition, the human response to mixtures of pathogens is poorly understood and needs more research. **Box 2** lists some of the other challenges to performing dose-response studies.

Outbreaks that are properly investigated in a timely manner may provide dose-response information. Data from outbreaks of waterborne disease reflect the populations of concern and exposures under real world scenarios. The challenge is to collect timely data on pathogen concentrations and exposures during the outbreak. Methods and incentives to better collect this kind of information from outbreaks need to be developed.

Animal models may be capable of predicting physiological events and health outcomes in humans, but the efficacy of these models has not been fully explored. If valid animal models can be identified, they can be used in dose-response studies to explore factors that might influence susceptibility, such as age, immune competence, and the co-presence of other (non-infectious) microbes in the host. Goals for evaluating animal models should include:

- **Examining different hosts.** Additional research will be needed to clarify the variability of infectivity of pathogens in different strains of animal hosts. Host markers will need to be compared between susceptible animal hosts and humans.
- **Evaluating possible physiological models.** Research should characterize the different barriers to infection (e.g., humeral and cellular immunity) in animal models and seek to compare the efficacy of these barriers to similar barriers in humans.
- **Evaluating the importance of prior pathogen exposure.** Research is needed to quantify the effect of prior exposure to a pathogen on susceptibility and response to infection.



- **Resolving scaling issues.** Research needs to address whether allometric methods (the comparative study of size, shape, and function in organisms) can be used to extrapolate dose information from animal models to humans.

There is growing pressure from the public to bring an end to all forms of animal testing, including using animals for modeling human diseases. Researchers must begin to explore animal-free modeling, including tissue cultures, three-dimensional cell systems and other *in vitro* assays, so that the results of these assays can be compared and validated against animal models before animal testing is banned. In addition, there may not be substitutes for human models where there are infections or disease endpoints only observed in humans.

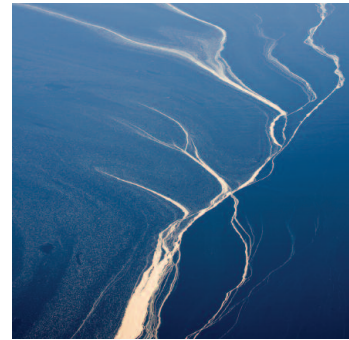
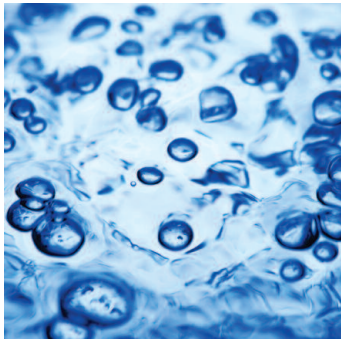
## OPPORTUNISTIC PATHOGENS

Opportunistic pathogens present a challenging problem for microbial risk assessment, because they only cause illness in a relatively small subset of susceptible people and are often found in the “normal” flora of healthy individuals or in the environment. Also, it is often difficult to distinguish opportunistic pathogens that were contracted from water or another environmental source from pathogens that emanate from the individual’s own normal flora.

In general, exposure to waterborne opportunistic pathogens is poorly understood and needs further research. Specifically, studies are needed to determine the contribution of environmental sources (including recreational water) to the carriage of opportunistic pathogens and to uncover dose-response relationships for opportunistic pathogens among susceptible populations. It is possible that colonization of a host by opportunistic pathogens could lead to increased susceptibility to other pathogens, but this remains to be explored.

## TRAINING, EDUCATION, AND COMMUNICATIONS ISSUES

Education and public communication efforts are critical to the successful implementation and application of the results of microbial risk assessments. For the field to make greater inroads into presentation of waterborne disease, the current cohort of microbial risk assessors must



be followed by a new group of scientists with cross-disciplinary training. Because microbial risk projects call on the skill sets of many different fields of expertise, microbial risk projects must involve collaboration across disciplinary and national boundaries. Finally, it should be remembered that microbial risk assessment is not limited to laboratories and classrooms. It must also include effective communication with water consumers.

#### **GAPS IN THE TRAINING OF RISK ASSESSORS**

Microbial risk assessment calls on the knowledge sets of many different disciplines. Cross-training and integration of people from such varied fields as microbiology, infectious disease medicine, epidemiology, modeling, engineering, hydrology, chemistry, health education, health promotion, behavioral science, policy, law, statistics, economics, and decision analysis is critical for carrying out meaningful measures of microbial risk.

Currently, there are a number of gaps in microbial risk assessment training. In addition to multidisciplinary training, risk assessors should

introduction to microbial risk assessment, the basics of modeling, and statistics. Web-based water utilities resources, like those used in the European Union (<http://smas.chemeng.ntua.gr/miram/>), could serve as suitable models for training modules in microbial risk assessment.

Since microbial risk assessment is usually included within the context of broadly-scoped projects, there is a lack of funding for training in microbial risk assessment-focused work. It may be possible to secure some funding for risk assessment training from industry.

At the undergraduate level, instructors need access to introductory microbial risk teaching materials and textbooks.

#### **NEW COLLABORATIONS**

Since microbial risk assessment involves many different areas of expertise, bringing diverse professionals together and uniting their skills is important, but it isn't always easily accomplished. For example, potential collaborators may not be aware of microbial risk assessment

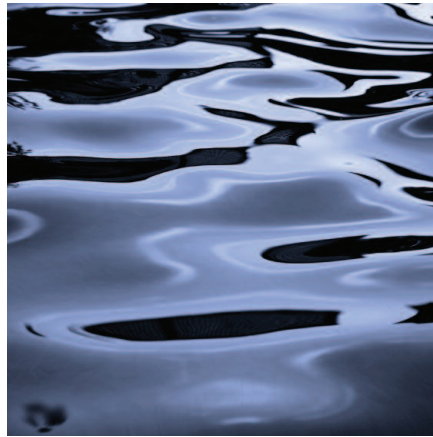
## **ANY RISK ANALYSIS THAT MIGHT BE USED TO SUPPORT REGULATORY DETERMINATIONS SHOULD HAVE BROAD STAKEHOLDER INPUT, TRANSPARENCY, AND INDEPENDENT REVIEW.**

have the benefit of specific preparation, but education in this field is patchy, and better coordination and standardization is needed.

Training and short courses are needed for professionals. Graduate-level courses offered by the Joint Institute for Food Safety and Applied Nutrition and the Center for Advancing Microbial Risk Assessment (see **References**) could serve as a good model for this sort of instruction. Also, professional associations could offer workshops to provide an

or how and under what circumstances it is used. However, microbial risk assessment is extremely effective when designed and carried out by multidisciplinary teams of professionals, so efforts to incorporate scientists across disciplinary boundaries are highly recommended.

Partnerships between universities and governmental units interested in microbial risk are also recommended. University and private sector scientists involved with microbial risk assessment are encouraged to



participate in government advisory boards and stakeholder and consumer associations. Any risk analysis that might be used to support regulatory determinations should have broad stakeholder input, transparency, and independent review.

International collaborations (like those coordinated through the WHO) in microbial risk assessment are critical for a number of reasons. Such collaborations can prevent scientists from duplicating their efforts on issues of common interest. Also, different countries possess different scientific strengths, and cross-border collaborations pull together the assets of many nations. Collaborations can help get an investigation off the ground in financial terms, as teaming with developing countries can attract funding from previously uninterested sources. Finally, international collaborations can force microbial risk experts to harmonize the terminology of the discipline, a bonus for the field as a whole.

## **MICROBIAL RISK ASSESSMENT AND PUBLIC EDUCATION**

Water consumers are the most invested stakeholders in water quality issues, but in the U.S., many consumers take safe water for granted and more or less ignore mailings that communicate water quality information. If water quality standards are not protective of all segments of a population, then specific subgroups need to be aware of potential risks so that they can take steps to protect themselves. Also, open lines of communication between water authorities and the public lay the groundwork for a cooperative relationship if an adverse event occurs. Public communication is often a necessary component when securing research funds. For instance, the National Institutes of Health, which supports many microbial risk assessment projects, has a new policy that requires “health promotion and health education” components in all of its research proposals.

The general public knows relatively little about microbial risk and assessment, so public communication about water related risks should be presented in an appropriate context. This information can be very basic. For example, people should know the basics about their water supply (the

source, type of treatment, and basic water quality results), what future treatment and infrastructure upgrades are necessary (and, hence, why consumers will need to pay for these costs), and why constant vigilance is required. Other helpful public information includes an explanation of why proper maintenance of home water treatment devices is important. The public should be given the opportunity to learn more about microbial risk through promotion of the EPA drinking water website.

Messages about waterborne risks need to come from trusted sources, including physicians and the health care community. Consumers are continually exposed to marketing messages from vendors of bottled water and water treatment devices, so it is important to balance these messages with reliable, unbiased information that can help consumers make informed decisions.

To help consumers understand the scope of the risks associated with drinking water, it may be useful to compare those risks with comparable hazards that are more familiar. Also, it would be useful to understand the public’s mental models about water-related issues so that communicators can grasp consumer perceptions and tailor messages accordingly. Uncertainty is part and parcel of microbial risk assessment, but conveying a sense of the uncertainties involved in estimating water quality to the public can be difficult.

Although communicating health risks to the public is important, there is inevitably a certain fraction of the population that will not want to receive communications. Engaging this sector may require careful timing. Different communication strategies will probably be needed for different segments of the population.

The scientific community can help improve public communication about waterborne microbial risk in a number of ways. Scientists should seek training to improve their outreach skills and reach out to the public, risk managers, the media, the medical community, and other stakeholders. Also, communication strategies, and risk communication in particular, should be part of every microbial risk assessment.

# Recommendations



- Microbial risk assessment, when properly and iteratively done, is a valuable tool. It can allow risk managers to develop a systemic platform for organizing and evaluating available data for establishing risks and evaluating competing, accumulative, or even delayed risks. Multiple iterations of a microbial risk assessment are encouraged as a learning tool to refine and test the risk assessment process.
- Numerical guidelines, such as EPA's microbial water guidance of one illness per 10,000 individuals in a given year, are useful benchmarks, but may not be suitable for all water exposures. The standard was derived based on observed illnesses, not subclinical infections. Additional research is needed to validate the guideline and to ensure that it reflects a realistic goal.
- The process of setting water quality standards should strive to include responsibility for developing and implementing special methods to protect sensitive subpopulations. That being said, equitable standards are meaningless if society cannot afford to meet them.
- The currently available indicator organisms are not adequate for developing microbial risk assessments of water. Microbial risk assessments should instead rely on measurements of the presence of specific pathogen strains for extrapolating risk. Rapid, inexpensive, easy to use, and easy to interpret analytical methods for specific pathogens or "marker" pathogens are necessary to provide a robust capability in this area.
- Microbial risk assessment needs to broaden the use of available epidemiologic data. Studies are needed to integrate outbreak data to better estimate microbial infectivity under real-world conditions; and to evaluate infectivity and dose response for waterborne pathogens.
- In general, safety factors should be avoided in microbial risk assessment. It is more appropriate and scientifically defensible to deal with uncertainty explicitly within risk management rather than to assign arbitrary safety factors for susceptible populations. Probabilistic distributions of risk may be used to express the uncertainty in an assessment. Safety factors, if they are used, should be part of a policy decision and separate from a risk analysis.
- An international database of readily assessable pathogen occurrence in drinking water and ambient waters should be established. Making data of this kind more widely available would inform microbial risk assessment and risk management and enable the implementation of effective public health initiatives.
- There is a pronounced need for improved monitoring designs that can capture spatial and temporal variability in pathogen populations. There is a need for more data and analytical techniques that can inform microbial risk assessments about such variations – especially for variations in water quality in drinking water distribution systems.
- The dose-response relationships for many important waterborne pathogens have not been determined and research is needed to address this deficit. Variability in dose-response results among the strains of the same pathogen should also be investigated.
- Credible animal models need to be developed. Although animal models may be capable of predicting physiological events and health outcomes in humans, the efficacy of these models requires more research. In addition, researchers must begin to explore animal-free modeling, including tissue cultures, 3-D cell systems and other *in vitro* assays and validate these approaches to animal and human models.
- An independent microbial risk assessment advisory board with members from both industry and academia (based on the model of the National Advisory Committee on Microbiological Criteria in Foods), and with international representation, should be assembled. An advisory board could foster the more consistent use of the best techniques for evaluating the problems of public health and ambient water.
- The general public needs to know basic information about their source and treatment of drinking water, the need for future treatment upgrades and infrastructure enhancements, and the fundamentals of microbial risk and assessment. Public communication about water related risks should deliver information in the appropriate context.

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