Water-related infectious disease is a leading cause of morbidity and mortality worldwide. The lack of access to safe drinking water and inadequate sanitation, particularly in less developed countries, is associated with an estimated 1.7 million deaths annually. In the United States and other developed countries, application of the multibarrier approach for protecting and treating water supplies has led to the virtual elimination of waterborne threats such as cholera and typhoid. Nevertheless, illnesses associated with contaminated drinking water and recreational water continue to be reported.

The actual number of cases of waterborne disease is likely to be higher than the reported values due to a number of factors, such as the passive nature of the waterborne disease surveillance system in the United States and the difficulty in attributing illnesses to waterborne exposures. Scientifically sound assessments of the risks posed by exposure to pathogens in water are therefore critical for determining the effectiveness of current source water protection and water treatment practices, as well as the need for additional regulatory or nonregulatory measures to further ensure the safety of the nation’s water supply.

Chemical and microbial risk assessments are similar with respect to the fundamental need to evaluate health effects and exposures, with a clear articulation of assumptions and uncertainties. There are, however, a number of important differences that lend additional complexities to the assessment of microbial risks. Some of the most distinct differences relate to the exposure component of the assessment. Unlike chemicals, microorganisms are typically not uniformly dispersed in the environment. The viability, virulence, and

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infectivity of species or strains of specific pathogens may vary considerably, and illnesses may be spread from person-to-person by secondary transmission. In the absence of robust data on these and other factors, as is commonly the case, many assumptions are required and the level of uncertainty in the assessments is likely to be high.

**Assessing Exposure to Waterborne Pathogens**

Ingestion of contaminated water or food represents the main route of exposure to waterborne pathogens, although inhalation of aerosols and dermal contact may also be important in some instances. Pathogens that may be transmitted through contaminated drinking water or recreational water include a wide range of enteric bacteria (e.g., *Escherichia coli* 0157:H7, *Campylobacter*, *Shigella* spp.), viruses (e.g., norovirus, hepatitis A, enteroviruses), and protozoa (e.g., *Cryptosporidium*, *Giardia*), most of which are commonly associated with acute gastrointestinal illness. Secondary transmission, host susceptibility, and behaviors such as water consumption rates and showering habits are important factors that can influence exposure and disease outcome.

**Sources of Waterborne Pathogens**

Groundwater and surface water (e.g., rivers, lakes, oceans) may become contaminated with pathogens wherever they come in contact with animal or human fecal wastes (see Figure 1). Wastewater treatment plant and septic system failures may lead to the introduction of pathogens into drinking water sources or recreational water. Heavy rainfall can cause runoff of fecal contamination from farm animals, and may lead to combined sewer overflow discharges to water bodies in some communities. Although a number of animal fecal pathogens are associated with human disease, many others of public health concern are host-specific. Human-specific pathogens often cause illnesses that are more severe and usually have low infective doses. The ability to differentiate between microbes of human, animal, and natural origin by phenotypic and genotypic tests can therefore be of considerable value in determining the potential risk that may be posed by strains detected in water samples. Drinking water distribution systems themselves may be a “source” of pathogens in biofilms that grow on the surface of the pipes.

**Pathogen Occurrence**

Estimates of exposure to a waterborne pathogen have traditionally been based on a simple determination of the occurrence of the target microbe or an indicator in a representative water sample. Occurrence values should be considered in the context of the many variables that can influence exposure of a susceptible host. The presence of pathogen in water is strongly influenced by the characteristics of the watershed. Microbes exhibit temporal (including seasonal) and spacial variability, and their ability to survive and multiply in the environment varies considerably. Detection methodology issues and the characteristics of the pathogen can also have an impact on estimates of exposure.

The presence of pathogens in water is usually quite low and the detection of pathogens of concern can be technically challenging. The performance of sample concentration, purification, and analytical methods therefore has a major influence on the reliability of occurrence estimates. The concentration and recovery of pathogens from large volumes of water by various physical and chemical separation methods is an essential first step. Highly efficient procedures are particularly important for viruses and parasites, which cannot grow outside their hosts. Despite recent advancements in this area, the need for more cost-efficient and easy-to-use
methods remains a high-priority research need.

A variety of techniques are available for pathogen detection and characterization once the sample has been concentrated and cleaned up to remove as many nontarget microbes and other interferences as possible. Methods for bacteria typically involve growing the target pathogen on selective culture media, and using biochemical, immunological or genetic analyses (e.g., nucleic acid amplification by polymerase chain reaction [PCR]) for confirmation. Some viruses and protozoa may also be grown in cell culture using susceptible host cells. Molecular techniques, either in combination with or without cell culture, are providing a greater level of sensitivity and specificity than was available previously for pathogen identification and quantification. Advancements have also been made in the development of cellular, molecular, and whole animal approaches for characterizing the viability, virulence, and infectivity of microbial isolates. Further research to develop validated, cost-effective, and practical methods will be required before they can be routinely applied in occurrence studies and microbial risk assessments.6

Indicators
An important issue in microbial exposure assessment relates to the use of fecal indicator organisms (e.g., fecal coliforms, *Escherichia coli*, enterococci) or chemicals as markers of fecal contamination and surrogates for pathogens of public health concern. The ideal fecal indicator has the following characteristics (1) present in the feces of humans and warm-blooded animals, and indicative of the potential presence of pathogens; (2) easy to detect and enumerate; and (3) survival in the environment and during water treatment is similar to, if not greater than, waterborne pathogens. The demonstration of a correlation between levels of an indicator and adverse health effects in humans is a particularly desirable quality, as has been reported in the U.S. Environmental Protection Agency’s (EPA) recreational water epidemiology studies involving the use of a quantitative PCR method for *Enterococcus* spp.7 Although some in the scientific community argue for a greater reliance on monitoring for specific pathogens rather than on indicators, the latter have been used with considerable success along with other water treatment and protection practices by the water sector for decades.

Host Response as Markers of Exposure
Antibody responses to selected pathogens, particularly *Cryptosporidium*, have been found to be of value as markers of exposure in outbreak investigations and clinical studies.8 The complexity of the immune response and the multiple sources and routes of transmission of waterborne pathogens, however, present some challenges to the use of this approach as a means to assess exposures. Nevertheless, the use of cellular and/or humoral responses to infection, as measured in biological specimens with various immunological and chemical assays, can be a more sensitive indicator of exposure than the often imprecise and inefficient approaches for direct detection of the pathogens in the environment. For example, Li and Dufour9 recently reported that interferon-γ produced by memory T cells was a highly specific marker of exposure to viruses in an animal model. Noninvasive approaches for obtaining clinical specimens, such as through the collection of saliva and measurement of secretory antibody, can be used as simple diagnostic tools to assess waterborne infectious agents.10,11 These types of biomarkers of exposure represent a promising new area of exposure assessment that may help overcome some of the limitations of the current tools for identifying waterborne pathogens of public health concern.

Summary
The conceptual framework for assessing risks to waterborne pathogens is inherently different than that used for chemicals due to the many unique features of biological contaminants and the way in which they interact with the environment and their human hosts. A comprehensive assessment of exposure to these agents requires a thorough understanding of the characteristics of the pathogen, the influence of the environment on its occurrence, and the response of the human host to infection (as it informs exposure). Reducing the uncertainties associated with exposure assessments in the future will require the continued development of more refined and cost-effective methods for concentrating, purifying, and analyzing waterborne pathogens and their indicators, along with a better understanding of the environmental and host factors that impact exposure and disease outcome.

References