Assessing the Risks Associated With Exposure to Waterborne Pathogens: An Expert Panel’s Report on Risk Assessment†

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ABSTRACT

The resurgence of outbreaks of waterborne diseases in the United States underscores the need for quantitative methods for assessing the human health risks associated with various types of waterborne pathogens in diverse environments (e.g., drinking water, waste water, recreational water) under different exposure scenarios (e.g., ingestion, inhalation from aerosols). An expert panel developed a three-stage general framework for conducting risk assessments of waterborne pathogens. An initial problem formulation stage involving all stakeholders identifies the purpose of the risk assessment, the critical issues to be addressed, and how the results might be used to protect public health. The analysis characterizes both the exposure and the health effects. This compilation of quantitative and qualitative data, expert opinion, and other information yields a host/pathogen profile that explicitly identifies the assumptions and uncertainties associated with the profile. The final stage, risk characterization, states the likelihood and types and magnitude of effects likely to be observed in the exposed population under the expected exposure scenario, including all the inherent assumptions and uncertainties. This characterization will be used by risk managers and policy makers to reduce human health risks and by risk communication specialists to inform the public.

Key words: Risk assessment, waterborne diseases, waterborne pathogens

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Until recently, people in the United States and other industrialized nations largely considered the problem of waterborne diseases to be unique to the developing countries of the world or to those ravaged by poverty or war (5, 6). However, with the outbreak of cryptosporidiosis in Milwaukee in 1993 (11), the public and the scientific community were reminded that waterborne infectious diseases are a clear and persistent threat to public health in this and other industrialized countries. In fact, outbreaks as well as sporadic cases of waterborne diseases have been an ongoing, but often unrecognized, problem in the United States for many years (5, 10). Recognition that infectious agents in drinking water, recreational waters, and other aqueous media to which humans may be exposed constitute tangible threats to human health (12, 19) has resulted in increased interest in the development of approaches to assessing the health risks associated with waterborne pathogens.

Human health risk assessment is a process leading to the “characterization of the potential adverse health effects of human exposures to environmental hazards” (13). Risk assessment identifies how humans might respond to agents in the home, workplace, and environment based on available information. This information may be qualitative or quantitative or may combine elements of each. The scientific basis and the process for conducting risk assessments evolved over many years, principally in the context of understanding the human health risks associated with exposure to chemicals. Chemical risk assessment, which was endorsed and codified by a committee of the National Research Council (13), consists of four steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

In chemical risk assessment, information relative to the first two steps, hazard identification and dose-response assessment, is obtained principally from animals exposed to the chemical of interest but may include data from human epidemiological studies and/or occupational exposure data when available. The third step, exposure assessment, addresses what is known about likely human exposures. This would include determination of where the exposure is likely to occur (e.g., in the home, workplace, or environment), the route of exposure (e.g., inhalation, ingestion, dermal contact), and the concentration(s) of the material. Finally, the risk characterization step integrates all of this information into a coherent and cohesive statement identifying, to the extent possible, the specific risks to the exposed population.

The chemical risk assessment approach has been used as a model for initial efforts to perform risk assessments for waterborne pathogens (7, 8, 15, 18). These efforts typically have sought to obtain point estimates of the probability of infection by specific pathogens without addressing the uncertainties associated with the estimates. It was suggested that a number of factors unique to pathogenic organisms could confound this application of the chemical risk assess-
ment model (8, 15, 18, 20). These include factors such as spatial variation in the concentration or density of the pathogens in the source water, temporal and seasonal changes in their patterns of distribution, secondary transmission of infection, concerns about interindividual variability in susceptibility to infection, and the relationships between exposure, infection, immunity, and disease. However, thoughtful reflection suggests that similar, if not identical, factors are germane to chemical risk assessment. For example, chemicals are not necessarily uniformly distributed in an aqueous medium (e.g., a discharge plume from a point source), secondary exposures may occur (e.g., laundry workers handling chemical- or radiation-contaminated clothing), and individual responses to chemical exposures vary from person to person (e.g., not all smokers develop lung cancer). The principal distinguishing feature between chemical and pathogen risk assessment is that pathogens have the capacity to grow, reproduce, and participate in complex biological interactions that affect both the pathogen and the host.

Many of the issues of concern to those interested in waterborne pathogen risk assessment also are of concern to food microbiologists and sanitarians. Buchanan (1), Buchanan and Whiting (2), Roberts et al. (16), Rose et al. (17), and others have described initiatives and approaches to developing and applying risk assessment models to foodborne pathogens. Despite obvious common issues and information requirements, the development of risk assessment models for waterborne and foodborne pathogens has proceeded largely independently, in part reflecting the division of regulatory responsibility for water and food safety. Foodborne pathogen risk assessment models are being developed under the auspices of the Codex Alimentarius Commission (3), the World Health Organization (21), various national food safety agencies (4, 14), and others. Most foodborne pathogen risk assessment models are considered as tools that support the hazard analysis critical control point (HACCP) concept (1, 17) to ensure food safety from farm to fork. HACCP-like approaches have yet to be considered in the development of waterborne pathogen risk assessment models, and these models are intended to be broadly applicable to all types and uses of water, not just drinking water.

**CHARGE TO THE WORKING GROUP**

During 1995, the ILSI Risk Science Institute, in conjunction with the U.S. EPA’s Office of Water and the American Waterworks Association Research Foundation, convened a working group to critically examine approaches to risk assessment for waterborne pathogens. The working group (Table 1), composed of scientists from government, industry, and academia with experience and expertise in microbiology, virology, risk assessment, and related disciplines, was charged with developing a conceptual framework for assessing human health risks associated with waterborne pathogens. Such a framework would provide a model for organizing and characterizing information for performing pathogen risk assessments. Working group members considered validation of the framework as a distinct second step, to be addressed separately.

Recognizing that risk assessment is a dynamic and iterative process, the working group reasoned that as information accrues during a risk assessment, the framework should be sufficiently flexible to facilitate reformulation of the original questions confronting the risk assessors. It was also important to recognize that not only risk assessors,

**TABLE 1. Members of the ILSI Risk Science Institute Pathogen Risk Assessment Working Group**

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but also risk managers and other stakeholders have a role in the risk assessment process. The working group was asked to consider what questions are likely to arise during a risk assessment and what information will be needed to address those questions.

During the development of the framework, the working group was asked to consider a variety of potential sources of exposure to waterborne pathogens, including drinking water, recreational water, and sludges. They also were encouraged to look broadly at waterborne pathogens and to consider bacteria, viruses, and eukaryotic pathogens and address how humans interact with the pathogen at both the individual and population levels.

During the working group's deliberations, it became clear that a risk assessment should be predicated on an unambiguous statement of the purpose of the risk assessment, i.e., why it is being performed. The goal typically is to determine the potential human health risks associated with a specific exposure to a known pathogen such as *Listeria* or *Escherichia coli* or *Cryptosporidium*. Similarly, in cases in which the etiological agent may not be known initially, it is important to determine promptly the risks associated with exposure to that source. It is presumed that specific identification of the causative agent will come later, and may necessitate reevaluation of the critical questions to be addressed by the risk assessment. Finally, the goal of risk assessment might be to identify the critical points at which the pathogen or exposure to the pathogen might be controlled. As noted above, this latter point is often of particular relevance in the context of exposure to foodborne pathogens.

The working group recognized that much of the information needed to characterize both pathogen exposure and human health effects would be contingent on the availability and/or development of field and laboratory analytical methods and tools. Rather than attempting to define or evaluate existing and/or emerging methods or identify specific research needed to provide appropriate methods or tools, the working group focused on identifying information critical to the risk assessment process.

The conceptual framework (Fig. 1) developed by the working group for performing risk assessments of waterborne pathogens (9) consists of three critical steps. The first is a formulation of the problem. The second is an analytical step incorporating an exposure characterization and a human health effects characterization, recognizing that information associated with each characterization is not mutually exclusive and must flow freely between both compartments. The analysis step leads to the third step, the risk characterization that results in an estimate of the specific risk associated with a specific exposure scenario.

**PROBLEM FORMULATION**

Problem formulation is intended to identify the purpose of the risk assessment and the critical questions to be addressed and will reflect the concerns of the stakeholder community. This will define the boundaries in which the risk assessment is to be effective and will address how the information is going to be used to establish public policy or to stimulate regulatory activities to protect public health. For example, the problem formulation process would address whether certain segments of the population, e.g., pregnant women, the elderly or the very young, or the immunocompromised, need to be specifically considered during the risk assessment. During the problem formulation step, available scientific resources will be identified, including local or national experts from academia, industry, and government; relevant data and/or literature will be identified and compiled; and approaches for analysis and interpretation of the available data and information will be developed.

Evaluation of available data is critical to the effectiveness of the risk assessment, regardless of whether the data are quantitative, qualitative, or semiquantitative. In the absence of good quantitative information or where qualitative information is uncertain, the assumptions that surround the development, application, and use of such information in the risk assessment process must be identified clearly. The problem formulation step should lead to the construction of a conceptual model of the interactions between the pathogen or the medium and the defined human population.

**ANALYSIS**

The problem formulation step sets the stage for the analysis, i.e., characterization of both the exposure and the
human health effects, recognizing the iterative and interactive nature of these analyses. The working group divided both the exposure characterization and the human health effects characterization into four information compartments (Fig. 2), recognizing that the information associated with each is not mutually exclusive and that information should flow freely between the conceptual compartments. Exposure characterization must begin with characterization of the pathogen. This includes identification of the biological and biochemical features that facilitate its identification and define its taxonomic relationships to other organisms. In part, pathogen characterization will address the pathogen’s biology and ecology, its virulence and pathogenicity, and the route and mechanism of infection. Mechanistic information might include identification of the distribution of certain cell surface receptors on specific organs or tissues of the host that may be important in the induction of the infectious process. Pathogen characterization should consider the pathology and pathogenesis associated with infection, e.g., the tissues infected and the signs and symptoms of infection. The host specificity of the pathogen should be determined, and its potential for secondary transmission should be established. The risk assessor also would like to know if the pathogen is resistant to specific control measures, i.e., chlorination, bromination, or other types of water treatment processes, as well as its antibiotic resistance profile.

The risk assessor then examines what is known about the occurrence of the pathogen. Issues of concern include its spatial distribution in the water source and whether its distribution changes daily, seasonally, or in an otherwise measurable fashion. In addition, the size and dynamics of the pathogen population need to be determined as well as the environmental conditions required to support the growth and reproduction of the pathogen. In some cases it may be important to identify certain indicator organisms or surrogates that can be used to predict the distribution, abundance, etc., of the pathogen of concern.

Exposure analysis considers factors that underlie actual human exposure, recognizing that exposure may be associated with drinking water, recreational water, sludges, or other aqueous media. In addition to characterizing the source of exposure, it is necessary to determine the route of infection, e.g., ingestion of contaminated drinking or recreational water. Pathogens also may occur in aerosols associated with household water taps or showers or those associated with waves at the beach. It is important to determine the exposure dynamics, i.e., the exposure may be continuous or intermittent or of short or long duration.

An additional aspect of the exposure analysis is to identify the exposed population, including the demographic characteristics of the population at risk and their interaction with the contaminated water. For example, the exposed population might be children swimming in a river downstream of a dairy farm or immunocompromised patients served by a contaminated water supply. Part of the exposure analysis should address the possibility of secondary transmission of the pathogen and, where appropriate, characterize such exposures.

When all available information has been brought to bear on these issues, the risk assessor can create an exposure profile. The exposure profile provides a quantitative and qualitative description of the magnitude and/or patterns of exposure for the population, including those members who may be at the greatest risk. This may be a recapitulation of the information identified during previous steps or a synthesis of that information into a comprehensive statement of the likely exposure scenarios. Importantly, the exposure profile will identify all assumptions that were made in the development of the profile, including those associated with the supporting data, and all uncertainties that are associated with the exposure profile itself.

The second component of the analysis step is characterization of human health effects, which also has four informational compartments. As noted previously, there is considerable overlap in the information requirements for the exposure and human health effects characterizations; necessarily reflecting the dynamic and iterative nature of the risk assessment process. By addressing the same issue from different perspectives, the risk assessor gains additional insight into the strengths and weaknesses of the available information.

The risk assessor begins by characterizing those segments of the population most likely to be exposed to the pathogen and/or those most likely to be affected. For example, exposure may be limited to those swimming at a specific beach or served by a particular branch of the water distribution system. Symptoms may be observed only among infants, the elderly, or other definable groups. Data from previous disease outbreaks, surveillance programs, and clinical studies may offer insight into the demographics of infection and behavioral and/or social factors that help to characterize the exposed population. Although the working group recognized the genetic basis for individual differences in susceptibility to specific infectious diseases, little information is currently available to be incorporated into the risk assessment process. It is also important to characterize the health, nutritional, and immune status of the exposed

![FIGURE 2. Schematic representation of factors addressed in the analytical stage of human health risk assessments for exposures to waterborne pathogens. From Risk Analysis, 1996; 16(6). Used with permission of Plenum Publishing Corp.](image-url)
population because such factors can modulate the individual's response to the pathogen.

The actual health effects resulting from infection need to be described, including the relationship between the infectious agent of interest and human morbidity and mortality. For both obligate and opportunistic human pathogens, the risk assessor needs to know the signs and symptoms of infection/disease, their severity and duration, and the likelihood of recurrence or sequelae that may adversely affect those individuals. It would be valuable to determine whether exposure to the pathogen can elicit a protective immune response that would reduce the likelihood of subsequent disease recurrence. It is important to determine if the infectious agent is sensitive or resistant to antibiotics or other antiinfective drugs. The potential for secondary spread of the pathogen must be established. The impact of the infection and subsequent disease state on the quality of life should be determined, including the need for hospitalization, lost work time, and restriction of regular activities.

Consistent with the chemical risk assessment model, the pathogen risk assessor needs to address the dose-response relationship for the pathogen of interest in order to understand the relationships between dose, infectivity, and clinical illness. Such information may be derived from epidemiological and/or clinical studies. The establishment of dose-response relationships for pathogens is controversial and provides the impetus for much research. Underlying concerns include dose-to-target relationships (e.g., whether exposure to a single pathogenic organism is likely to cause disease), comparative infectivity of different strains and/or variants of specific pathogens, identification of appropriate measures of infectivity and disease, identification of defining clinical manifestations of infection and subsequent disease, and identification of specific markers of infection. These uncertainties also permeate the development and application of risk assessment models for foodborne pathogens (1, 2, 4).

By combining information that characterizes the exposed human population and the health effects associated with exposure to the pathogen of concern with information on the dose-response relationships, the risk assessor will be able to construct a host/pathogen profile. The profile incorporates all relevant quantitative and qualitative data gathered from the human health effects characterization process to identify and describe the likely consequences for human health of exposure to the pathogen of interest. Again, the assumptions inherent to the information incorporated into the host/pathogen profile need to be identified, and uncertainties associated with the profile itself should be clearly articulated.

RISK CHARACTERIZATION

Having carefully formulated the problem and performed the analytical steps leading to the development of an exposure profile and a host/pathogen profile, the risk assessor next prepares the risk characterization. This is a specific statement of the likelihood of effects in the exposed population given the exposure scenario derived from the exposure profile. The risk characterization will consist of a risk estimate describing both the types and magnitude of anticipated effects and the assumptions and uncertainties inherent to those estimates. When possible, statements about the underlying assumptions and the inherent uncertainties are expressed in quantitative terms, and their impact on the described risk assessment are identified and discussed.

The risk characterization step yields one or more risk estimates. These estimates reflect a weight of evidence approach that incorporates both quantitative and qualitative data, expert opinion, and other types of information. With such a diverse array of information, the risk estimates should be accompanied by a description of the degree of confidence the risk assessor has in those estimates. This description should specifically address the adequacy of the risk assessment relative to the issues and questions developed during the problem formulation step.

The resulting risk characterization is narrative in form and supported by quantitative and statistical data where appropriate. The risk characterization represents the final product of the risk assessment process and will be used by risk managers and policy makers to implement actions and policies that will reduce or minimize the estimated risks to the population. Risk management may take many forms, e.g., improved water treatment, water use/contact restrictions, development of alternative water sources, implementation of public vaccination programs, and will likely be determined on a case-by-case basis. The risk characterization will also provide the basis for communicating the risks to the affected community. This will be the critical information source that risk communicators and others will rely on as they interact with the affected community.

The development of this conceptual framework for assessment of the risks associated with exposure to waterborne pathogens is an important first step for the ad hoc working group. A number of issues were identified during the process that warrant closer scrutiny, e.g., pathogen detection methods and dose-response relationships. It is also clear that the only effective way to determine the utility of the framework and to identify its strengths and weaknesses is to use it in real world applications. Thus, this framework will serve as a challenge to the scientific community by identifying issues critical to the development and application of a risk assessment model for waterborne pathogens.

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WATERBORNE PATHOGEN RISK ASSESSMENT