Development of Incident-based Microbial Risk Assessment Framework

Charge to SAB Panel

Background:

The US Environmental Protection Agency's (EPA) National Homeland Security Research Center (NHSRC) has been established to conduct research in support of safe buildings, secure water systems and the rapid assessment of risk from exposure to highly virulent agents after a terrorist incident. In the event of a release of a biological agent, the EPA would respond in accordance with the Homeland Security Presidential Directives 7, 9 and 10 (http://www.epa.gov/homelandsecurity/htm/ohs-sp.htm). EPA has mandated roles in decontamination, water infrastructure protection, and risk assessment. HSPD 7 designates the EPA as the sector-specific lead agency for critical water infrastructure safety and security. HSPD 9 addresses EPA's role in creating a fully-coordinated surveillance and monitoring program for early detection of bioagents as well as the development of a nationwide laboratory network to support routine monitoring and response requirements. HSPD 10 mandates that EPA is the lead agency in decontamination efforts. The risk associated with a deliberate exposure situation is one of the drivers for decisions regarding evacuation, decontamination and eventual re-entry to a site or re-use of a water system. Thus, the NHSRC is faced with having to address critical scientific issues related to homeland security.

The NHSRC's Threat and Consequence Assessment Division (TCAD) is responsible for assessing the health risks associated with the intentional release of hazardous and toxic materials including chemical, biological, radiological, and nuclear threat agents. To achieve this goal, the TCAD is currently developing tools, technologies, and methodologies to help prepare for and respond to acts of terror. The development of rapid and credible microbial risk assessment (MRA) methodologies that are transparent in explaining the limitations of the available data and the processes by which plausible inferences of risks and uncertainty are estimated is of major significance. MRA methodologies will be continually improved and enhanced by the TCAD as more data become available and additional information is gained regarding the mechanisms involved.

Currently, there is no consensus-based risk assessment methodology for evaluating biological contaminants and establishing clean-up levels following a large-scale environmental contamination. Thus, there exists an urgent need for the development of a preliminary decision-based framework as a tool to guide the conduct of risk assessments on a site-specific basis. In the absence of a scientifically-based, consistent, and transparent method for addressing and defending risk management decisions, the decontamination response is faced with cleaning-up to "zero" (i.e.. no visible growth in culture after surface sampling). The answer to "How Clean is Clean" is difficult to define for all biothreat agents (NRC, 2005) Thus, a "no risk" clean-up

goal is difficult, if not impossible to identify and achieve due to the lack of reliable and complete dose-response data as well as variabilities and uncertainties associated with sampling, decontamination and detection techniques. To begin the process to systematically gather site or incident-based information and assess the risks associated with contaminated areas after an incident, the TCAD has embarked on the-development of an incident-based MRA decision framework. The primary goal of the framework is to derive realistic and achievable acceptable risk levels (i.e., those that may be other than "zero-no growth in culture" as acceptable decontamination goals).

Previous efforts have laid the foundation for estimating health and environmental effects of microbial contamination (NRC, 1983; ILSI, 1996; ILSI, 2000; Haas et al, 1999; FAO/WHO, 2002; USEPA, 1992; USEPA, 1998). The basic tenets of conducting microbial risk assessment (MRA) overlap with that of chemical risk assessment. Generally, most microbial risk assessments use a modified version of the National Research Council's (NRC, 1983) framework consisting of four primary steps involving: 1) hazard identification, 2) dose-response, 3) exposure assessment, and 4) risk characterization. A problem formulation step was added in the International Life Sciences Institute Framework for Microbial Risk Assessment that defines the fundamental questions and the scope at the onset of the risk assessment process (ILSI, 2000). Similarly, the first step in the USEPA's Framework for Ecological Risk is a problem formulation step. The next phase in the Ecological Risk Assessment framework is analysis which consists of two activities: characterization of exposure and characterization of ecological effects. The framework uses characterization of ecological effects rather than hazard assessment because the term "hazard" is more relevant to chemicals than for non-chemical stressors (US EPA, 1998) and may not account for the dynamic interactions of biological processes within the environment. Likewise, estimating risks from microbial agents also must account for the dynamic infectious disease processes involved in direct and indirect exposures to microbes from the environment to persons and from person-to-person contact.

The risk assessment required to address consequence management and decontamination from biological contamination is challenging, particularly with respect to the ability of pathogenic microorganisms to infect and replicate in a host as well as be transmitted from host to host and/or transported in the environment. Quantitatively assessing risks from microorganisms and viruses is difficult due to the limited information on key characteristics such as infectivity, agent persistence, aerosolization potential, and chlorine inactivation compounded with the replication, genetic variability, and secondary transmission which are unique to each microorganism. Additionally, modern sampling techniques employing molecular analyses may overestimate the risk if they are not combined with culture methods to assess viability.

Review Material:

The Threat and Consequence Assessment Division has prepared a white paper describing the issues regarding microbial risk assessment, development of cleanup levels and associated decontamination response, and the development of an incident-based microbial risk assessment framework.

Charge Questions:

The Threat and Consequence Assessment Division (TCAD) is consulting with the SAB to obtain advice on a framework addressing intentional biological contamination events. TCAD seeks comment on: 1) the approach to incident-based microbial risk assessment, 2) hazard assessment for a decontamination response, 3) exposure assessment for a decontamination response, and 4) how to address the uncertainties associated with microbial risk assessment.

Approach to Incident-based Microbial Risk Assessment:

1) Given the uncertainties of not being able to truly quantify zero with today's detection technologies, can a sound risk assessment methodology help in setting clean-up goals over than zero growth?

2) Should the output of the microbial risk assessment framework be developed to give quantitative or qualitative measure of risk?

3) Does the Incident-based Microbial Risk Assessment Framework represent a success-oriented approach to establishing clean-up goals?

Pathogenicity Assessment for Decontamination Response:

1) What are the key characteristics of microbial agents that represent the most important elements in a microbial risk assessment methodology?

2) If screening technologies have classified the agent (e.g., gram negative) and a decontamination technology has been verified to be effective for this class of organisms, is it necessary: a) to definitively identify the microorganism before implementing the decontamination technology, and b) to definitively identify the microorganism for clearance?

Exposure Assessment for Decontamination Response:

1) What are the key variables associated with Exposure to biologicals that represent the most important elements in a microbial risk assessment methodology?

2) Should host persistence be integrated into the exposure assessment?

3) Should the framework be developed to account for the dynamic infectious disease processes initiated *in vivo* that could result in multiple exposures and secondary transmission? How does one account for cumulative effects and/or replication of the organism in vivo?

Uncertainties in Microbial Risk Assessment:

1) How should background data be accounted for in deriving clean-up goals?

2) How should the uncertainties of extrapolating dose-response data from animal studies to humans be addressed? Impact of strain variations?

3) How should persistence or bacterial decay be addressed in the risk assessment framework?

4) How should the uncertainties associated with sampling efficacy and analytical detection be accounted for in the framework?

References:

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