91. Framework for Incident-Based Risk Assessment for Biothreat Agents

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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 5, 7, 9 and 10. EPA has mandated roles in decontamination, water infrastructure protection, and risk assessment. 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.

Although some of the basic tenets of conducting chemical risk assessment overlap with that of Microbial Risk Assessment (MRA), the EPA will be challenged when confronted with cleaning-up environments contaminated with biothreat agents (Canter, 2005). Quantitatively assessing risks from microorganisms 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.

Previous efforts in MRA have laid the foundation for estimating health and environmental effects of microbial contamination (ILSI, 1996; ILSI, 2000; Haas et al, 1999; FAO/WHO, 2002; USEPA, 1992; USEPA, 1998). However, 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) because the answer to "How Clean is Safe" 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 (Figure 1). 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).

The preliminary MRA framework as presented here represents an on-going effort to provide an initial template and decision tool that addresses information gathering and decision support activity to develop risk assessments for sites contaminated with biothreat agents. Risk assessments are required in the short and long term. The MRA framework is organized as a three-tiered process to support initial site assessment followed by more in-depth hazard and exposure assessments as additional site and hazard information is accumulated from the ongoing investigations and sampling analyses.

This paper will provide an overview of the tiered approach being developed and proposed for use in responding to emergency situations.

Tier I: SITE ASSESSMENT

The Tier I Site Assessment enables a rapid, qualitative assessment of the situation and usually occurs within hours of the incident. Ideally, the contaminating agent would have been identified during the initial stages of the investigation and before the initiation of the Site Assessment by the environmental risk assessor. However, delays in analytical detection and/or latent symptoms in the exposed population may thwart rapid bioagent identification. Based on historical evidence from accidental and intentional releases and experimental studies, the first indication of a biological incident may be clustering of clinical cases in regions of high exposure (NRC, 2005). In addition to knowledge of the time, location and extent of contamination resulting from the release, information is also needed on contact rates (frequency, duration and intensity of exposures), possibly over an extended time interval if the release was not discovered until after clusters of exposed individuals began developing symptoms. The authors of this framework recognize that confirmation of the agent identity and its concentration may not be available within the time constraints for Tier I (several hours) such that certain default assumptions regarding the identity of the biological threat agent will be necessary. For example, in the absence of definitive agent identification, initial assumptions could be based on available physical data and the mode of delivery until more reliable data are acquired.

The next steps in the Tier I Site Assessment are designed to determine the extent and nature of the contamination. Potentially, the extent of the contamination could be determined rapidly with a sufficient degree of certainty from the initial screening samples using a targeted sampling plan and rapid bioagent detection test kits. Determining the fraction of positive samples and their location within a building or water distribution system is important in bounding the area of contamination and identifying any hidden recesses where decontamination agents may not easily reach the biological organism. Depending on the time constraints and the available data, the MRA framework identifies additional data gathering steps such as location(s) of release and time(s) of delivery associated with environmental parameters and human receptors. Information to enable additional supplemental site characterization include: architectural or engineering drawings; maps of ventilation and water systems; recirculation and

exhaust rates; filtration or treatment systems; climatic conditions; and information on adjacent or neighboring sites of concern for transmission. The acquisition of this additional information supports the fact that exposures to the identified biothreat agent can occur or have occurred on the site.

The outcome of Tier I is a preliminary narrative that communicates, in the short term, what is known (and not known) about:

1) The characteristics of the agent
2) The characteristics of the symptoms or effects detected
3) The potentially exposed population
4) The assumed extent of contamination
5) The assumed extent and possible spread of effects
6) The potential for any observed adverse health effects in the potentially exposed population
7) The persistence of the biothreat agent based on the mode of delivery and the environmental factors associated with the release

Potential circumventions or default assumptions, as well as some resources for data input and derivation will need to be applied when data are insufficient or not available from the site investigation. When communicating the Tier I Site Assessment to risk managers and stakeholders, transparency is extremely important. The risk assessor must acknowledge the quality and availability of the information known and the default assumptions with the level of uncertainty upon which the Site Assessment was developed.

Tier II: SCENARIO ASSESSMENT Overview

Tier II Scenario Assessment may be triggered by several events or conclusions including: (1) the Tier I narrative site assessment suggesting a human health risk exists that must be further characterized; or (2) decisions regarding remediation or site re-entry are needed. Tier II is a multi-leveled, dynamic process that provides a more extensive approach for incident-based site assessment and requires site-specific data to support science-based risk management decisions, such as decontamination goals for reoccupation of the site or utilization of the water distribution system. In Tier II, the risk assessor "drills down" through two parallel processes: the Exposure Assessment (EA) and the Hazard Assessment (HA), as required, with increasing site-specificity and data intensity as additional scenario-based data are acquired. Tier II begins to quantify the risks associated with the exposure or potential exposure.

Tier II: EXPOSURE ASSESSMENT

The objective of the exposure assessment (EA) is to estimate the degree of exposure (quantitatively) and determine routes of exposure and potential pathways (U.S. EPA, 1989). Exposure assessment is a key component in both the Tier I rapid site assessment and the Tier II quantitative risk assessment for contamination of buildings and water distribution systems with biological agents. The Tier II EA builds upon the information gathered in the Tier I assessment and supplies information to the Tier III risk characterization. Tier II EA further delineates potentially contaminated areas and identifies groups of individuals that are likely to come in contact with the agent, refining the preliminary recommendations generated in the rapid Tier I site assessment and incorporating the evolving scenario data.

The six steps in the Tier II EA (Figure 1) can be categorized into three groups. The first group consists of Steps EA-1 and EA-2, which re-examine the initial data and assumptions from

the Tier I Site Assessment and identify the data gaps. The second group consists of Steps EA-3 through EA-5, which are iterated until Data Quality Objectives (DQOs) (Figure 2) for the site are achieved. The third group consists of Step EA-6, where dose exposures are estimated and incorporated into the risk characterization.

To determine the nature and extent of contamination at a site or in a system, a combination of operational and statistical models can be used to achieve this objective. The purpose of the models is to predict the distribution of microbial agents within buildings, water systems, and outdoor environments, and to aid in the selection of sampling locations (e.g., to collect samples from areas where agents are predicted to occur in the highest concentration). Defaults are proposed for some characteristics of the release-exposure scenario (e.g., form of release) model inputs and model parameters. The development of innovative approaches to generate default values for the agents' distribution, infectivity potential and other relevant characteristics is an on-going effort to continually adjust for key data gaps as they are identified and maintain forward progress of the risk assessment process. The potentially exposed populations and their activity patterns must be defined so that all exposure pathways are identified. The MRA framework considers three exposure pathways: inhalation, ingestion, and dermal. If the existing data (i.e., data generated in Tier I) do not allow estimation of exposure concentrations with the accuracy and precision required to support decision-making, and then an environmental sampling plan must be developed. Sample collection efforts in air, water and on surfaces are envisioned to be iterative. The sampling effort is anticipated to employ field-based analytical methods and data analysis (when feasible) that continues until the requirements developed during the Data Quality Objective process (Figure 2) required by the EPA are achieved. The estimation of exposure concentration serves to refine site boundaries and may be ranges of concentrations or estimates of distributions of concentrations. An assessment of the uncertainty in the estimate should be provided. The output of the EA is the estimation of point estimates, distributions, or ranges.

Exposure assessment inherently contains uncertainties associated with estimating the magnitude of exposure (i.e., due to sampling and analytical errors) and estimating values for exposure factors that affect the intake estimate. These uncertainties complicate the site risk management decisions, such as whether to evacuate a building, which areas require abatement, and when the building may be cleared for re-entry.

Tier II: HAZARD ASSESSMENT

Three critical factors interplay in the infectious disease process – a susceptible host, an available pathogen, and favorable environmental conditions resulting in exposure (Figure 3). The hazard assessment (HA) approach presented in the MRA framework makes use of these variables in two steps: Hazard Identification (HID) and Dose-Response Assessment (DRA). A systematic analysis of relevant health effects data is required for both HID and DRA.

The body of knowledge for the HA is compiled from databases and from information contained within published and unpublished scientific studies on biothreat agents, or on potentially-related agents (such as surrogates), in the absence of sufficient data. It is recognized that the use of surrogate data may increase the uncertainty of the resultant outcome both qualitatively and quantitatively. However, in the absence of data, this default approach may be necessary to inform decision-making. Research into the use and applicability of surrogates is being conducted to inform the process and identify when the use of data may or may not be appropriate.

The first step of the HA is Hazard Identification (HID) which is a further delineation of the qualitative aspects of the assessment of data that identifies the potential human health hazards associated with the exposure scenario of concern (agent, route, duration). The qualitative information gained in the initial stages of an incident through Tier I Site Assessment will guide the Hazard Characterization step, which evaluates the key characteristics of the hazardous agent. Among the key characteristics are factors that enhance virulence and/or environmental stability. The next step, the DRA, involves an analysis of the relationship between the dose received and the respective response. For biothreat agents, appropriate dose-response data for the human population are limited and, in many cases, dose-response estimates must be based upon extrapolations from animal studies and/or studies conducted with surrogate agents. One of the greatest challenges of any risk assessment is to quantitatively extrapolate results from animal studies to the human population. Animal studies are often administered at intentionally high doses to achieve effects; however, lower doses are needed to estimate safe levels to guide the detection and decontamination processes. Animal studies may not be good predictors of the human situation and oftentimes, may not be available for the appropriate route of exposure. Such uncertainty must be captured and incorporated into the resulting assessment to enable responsible decision-making. Additional considerations in estimating response from exposure include extrapolations across exposure durations, transmissibility from inanimate objects to human host and/or host to host (e.g. human to human, animal to human), pathogen strain, severity of effects, susceptible subpopulations, exposure route and/or exposure duration. The framework identifies and considers different options for modeling the available dose-response data and assumptions for the biothreat agents based on the key characteristics known for the bioagent.

Tier III: SCENARIO RISK CHARACTERIZATION

The final step in the Microbial Risk Assessment Framework is Risk Characterization (RC), which is a synthesis and summary of the incident-specific data assessing the risk of bioagent contamination to the environment and exposure to the affected population. Risk characterization integrates the hazard and exposure components of the risk evaluations in Tiers I and II. It is important that all steps in the risk assessment are transparent; therefore, the Risk Characterization step includes a description of the assumptions, scientific evidence, and uncertainties that are used in evaluating the incident data. Due to the time constraints associated with a biothreat event, the Risk Characterization step will involve evaluating and integrating the data derived from both the site through Tier I Assessment and the more in-depth hazard and exposure analysis in Tier II. The output of the Risk Characterization provides the risk managers and stakeholders with scientifically-based information upon which rapid decisions can be made to protect the health of the exposed population and to effectively and economically remediate a contaminated environment.

SUMMARY

In the event of an emergency situation, agencies and organizations, as dictated by Homeland Security Presidential Directives 5, 7, 9, and 10, will look toward EPA for leadership and decision-making in determining contaminant levels requiring immediate evacuation as well as decontamination levels to permit re-entry of contaminated structures or sites and resumed use of contaminated water systems. Recognizing the urgent need for a rapid microbial risk

assessment process, NHSRC has developed a preliminary incident-based biological framework to address the scientific and decision options in a methodology aimed at enabling the assessment of risks of exposure to intentional, accidental, and natural microbial contamination. The three-tiered framework is organized to support rapid risk management decisions from preliminary site-specific data gathered during Tier I, followed by a more thorough risk evaluation in Tier II as more reliable site-specific data are received, culminating in a Scenario Risk Characterization in Tier III. In order to guarantee continued development of the risk assessment while having to accommodate incomplete data on the biological threat, the framework recognizes and encourages the use of innovative default approaches to bridge key data gaps in biological agent characteristics identified throughout various phases of the information gathering process.

KEY WORDS
Microbial risk assessment, biothreat agents, hazard assessment, exposure assessment, risk characterization, transmissibility

FIGURES
Figure 1: Overview of Incident-based Microbial Risk Assessment Framework
Figure 2: Data Quality Objectives
Figure 3: Critical Factors in Microbial Risk Assessment

REFERENCES
Canter, D. A. (2005) Addressing residual risk issues at anthrax cleanups: how clean is safe? J. Toxicol. Environ. Health A. 68(11-12):1017-32.

FAO/WHO (2002) Principles and and Guidelines for Incorporating Microbial Risk Assessment in the Development of Food Safety Standards, Guidelines, and Related Texts. http://www.who.int/foodsafety/publications/micro/march2002/en/index.html. Last accessed August 20, 2006.

Haas, C. N., J. B. Rose, and C. P. Gerba. (1999) Quantitative Microbial Risk Assessment. John Wiley & Sons. New York.

ILSI (International Life Sciences Institute) Pathogen Risk Assessment Working Group. (1996) A Conceptual Framework for Assessing the Risks of Human Disease Following Exposure to Waterborne Pathogens. Risk Analysis. 16:841-848.

ILSI (International Life Sciences Institute) Pathogen Risk Assessment Working Group. (2000) Revised Framework for Microbial Risk Assessment. ILSI Press. Washington, DC. Last accessed August 20, 2006.

National Research Council (2005) Reopening Public Facilities after a Biological Attack. National Academies Press. Washington DC

USEPA (1989). *Risk Assessment Guidance for Superfund.* (Rep. No. EPA/540/1-89/002). Washington, DC. (where is this reference cited? I don't think it is an appropriate reference given that it relates to chemicals unless you want to reference it in the first line of the second paragraph)

USEPA (1992) Framework for Ecological Risk Assessment. EPA/630/R-92/001F. Washington, DC.

USEPA (1998) Guidelines for Ecological Risk Assessment. EPA/630/R-95/002F. Washington, DC.

Figure 1: Overview of Incident-based Microbial Risk Assessment Framework

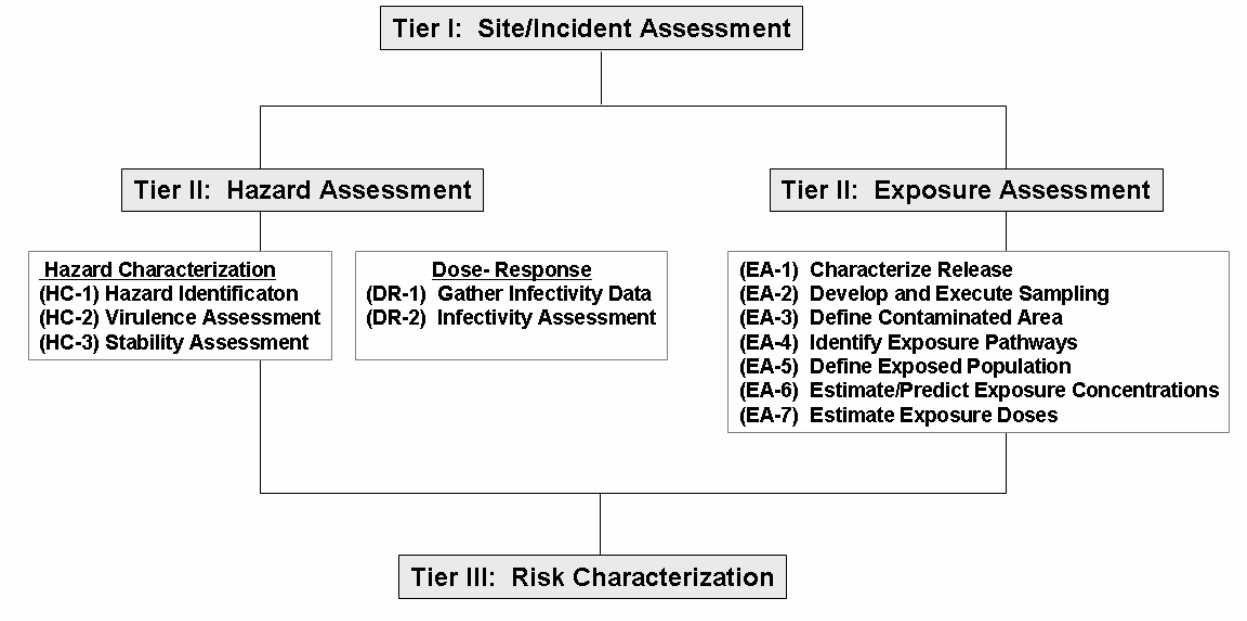
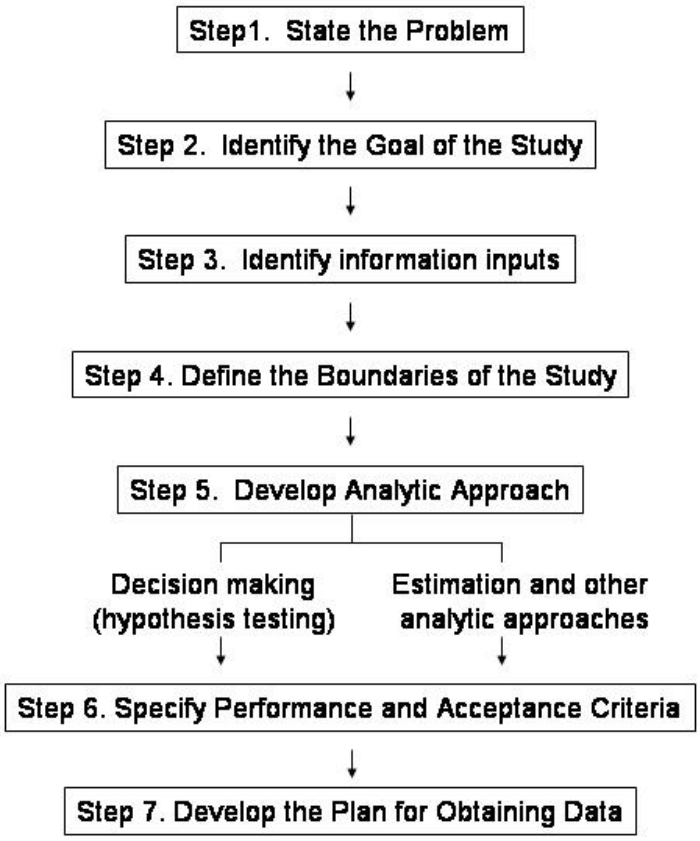


Figure 2. Data Quality Objective (DQO) Process



http://www.epa.gov/quality/qs-docs/g4-final.pdf

Figure 3. Exposure Factors affecting Infectious Disease Process