

**Risk Assessment of the
National Emerging Infectious Diseases
Laboratories
at the Boston University Medical Center**

NIH Blue Ribbon Panel

March 19, 2010

8:30 AM – 2:00 PM



Agenda Overview

- **Overview of the Supplementary Risk Assessment:**
 - **Development process**
 - **Recap of Recommendations from National Research Council and the Blue Ribbon Panel**
- **Proposed Approach for Modeling**
- **Modeling Transmission of Potential Infections**
- **Group Discussion**
- **Public Comment**

Goal of Today's Meeting

- **Provide status update on work accomplished to date on the supplementary risk assessment**
- **Seek NRC input at this key juncture in the development of the risk assessment on proposed strategies and methods for analysis**

Background

- In 2003, following a scientific merit, peer review process, BU Medical Center was awarded a grant from the NIAID to build a national biocontainment laboratory (NBL) known as the National Emerging Infectious Diseases Laboratories (NEIDL)
- The mission of the NEIDL is to:
 - Assist national, state and local public health efforts in the event of an infectious disease emergency or an act of bioterrorism
 - Serve as a national resource for conducting biodefense research to provide comprehensive, state-of-the-art biosafety level 2, 3, and biosafety 4 (BSL-4) research space
- Law suits filed in State court (July 05) and Federal court (May 06) to stop construction and operation of the NBL



Establishment of Blue Ribbon Panel

- **Providing scientific and technical advice to guide the agency in responding comprehensively to judicial requests and public concerns regarding the operation of the NEIDL**
 - **16 members**
 - **Expertise in ID and ID modeling, public health and epidemiology, risk assessment, environmental justice, risk communications, biodefense, and biosafety**

Specific Tasks

- **Determine what additional studies are needed to assess potential risks and public health consequences of:**
 - **Accidental and malevolent releases of infectious agents**
 - **Exposure to infectious agents in urban versus less populated locations**
- **Define the key elements of studies:**
 - **Infectious agents**
 - **Scenarios**
 - **Methodologies**
- **Address underlying concept of “worst case”**

Panel's Approach

- **Reviewed background materials:**
 - **Previous studies**
 - **Public input**
 - **Judicial materials**
 - **Epidemiologic and demographic data**
 - **Safety and emergency preparedness plans**
- **To further inform the Panel's analysis, the NIH engaged the NRC to suggest approaches to risk assessment**
 - **BRP/NRC Meeting May 2, 2008**
 - **BRP/NRC Teleconference April 7, 2009**
- **Continued consideration of comments and feedback received from the public, as well as input from the NIH Advisory Committee to the Director and Council of Public Representatives**

Blue Ribbon Panel Meetings

- **March 13, 2008**

- Discussed overarching aims and the scope of relevant research
- Federal, state, and municipal officials presented on pertinent research oversight requirements
- Reviewed summary of legal proceedings
- NIH presented an overview of the 2007 draft supplementary risk assessment

- **May 2, 2008**

- Invited the NRC to present their “Letter Report Regarding the Strategies to Address Issues Concerning the 2007 Draft Supplementary Risk Assessments and Site Suitability Analysis for the NEIDL”
- NRC provided additional input regarding the design and development of a subsequent risk assessment

Initial BRP Meeting with the Boston Communities

May 16, 2008

Massachusetts State House
Boston, Massachusetts

- Presented the BRP charge and proposed approach to supplementary risk assessment
- Most of meeting devoted to public comment session



Advisory Committee to the Director (ACD)

- **June 6, 2008**
 - **BRP recommendations regarding study design (agents, scenarios, and methodology) for a supplementary risk assessment were unanimously approved by the ACD**

BRP Meeting with the Boston Communities

July 16, 2008

National Institutes of Health

Bethesda, Maryland



- **Invited members of Boston community, Boston city officials, community researchers, and social justice experts**
- **Explored case studies on community engagement and environmental justice**
- **Roundtable discussion of how to effectively engage communities**

BRP Meeting with the Boston Communities

October 14, 2008

Hibernian Hall

Roxbury, Massachusetts

- **Engaged community members in planning of meeting and outreach efforts**
 - Broad multi-media public announcements
 - Evening meeting in local community hall
- **Presented, and sought community input on, draft principles and best practices for community engagement**
- **Heard general comments and perspectives from community members**



Advisory Committee to the Director

- **December 5, 2008**
 - **Provided a progress update to the ACD on the development of a subsequent risk assessment and BRP activities regarding community engagement**

Council of Public Representatives (COPR)

- **October 29, 2009**

- **The COPR is a federal advisory committee made up of members of the public, who advise the NIH Director on issues related to public participation in NIH activities, outreach efforts, and other matters of public interest**
- **COPR members expressed an interest in understanding the scientific and public health objectives of the NIH's research program in emerging and infectious diseases and in particular, the role of the NEIDL in supporting such research**
- **The work of the BRP was presented COPR members who offered valuable perspectives on community engagement**

NRC Committee on Technical Input on the NIH's Draft
Supplementary Risk Assessment for the Boston
University National Emerging Infectious Diseases
Laboratories:

NIH Requests Input from NRC

NIH Requests Input from NRC

- **The NRC Committee met with the BRP on May 2, 2008 to:**
 - **Discuss in greater detail overall concerns about the prior draft supplementary risk assessment**
 - **Provide perspectives on approaches to be taken and issues to be addressed in any future risk assessment**
- **NRC specific conclusions were consistent with the Panel's, validating its emerging findings**

NRC Recommendations: Range of Scenarios

- **Rather than worst case, two phases of analysis were suggested:**
 1. **Plausible scenarios designed to allow a realistic assessment of risks**
 - Procedural failures
 - Containment systems/ equipment failures
 - Malevolent actions
 2. **Credible high-consequence event for assessment**
- **Include probabilistic statements**
 - Empirically based if possible
- **Include mitigation capability/effects**

NRC Recommendations (Cont'd): Agent Selection

- **Select a variety of agents for assessment with appropriately diverse transmission characteristics**
 - **Portal: bloodborne, transmitted on fomites, spread by aerosol, and/or requiring vectors and the potential for maintenance in existing reservoir species**
 - **Aspects of transmission: high or low R_0 , latency, and incubation periods**
- **Clarify for the public and courts what agents and forms of agents will *not* be researched at the NEIDL (e.g. virus that causes small pox)**

NRC Recommendations (Cont'd): Consider Outcomes in Light of Agent Characteristics

- **A risk assessment should begin with the following four outcomes and assess how the characteristics of agents studied in the NEIDL might influence the likelihood of each outcome in the event of a release:**
 - **No subsequent transmission, following a small initial pool of infection**
 - **Little or no subsequent transmission, following multiple exposures**
 - **Limited transmission that is contained by public health measures**
 - **“Amplified” transmission**
- **Qualitative analysis of potential outcomes should consider impact of local characteristics (e.g. population density, vector availability, public health infrastructure) on the probability of the various outcomes**

NRC Recommendations (Cont'd): Modeling

- **Modeling is not mandatory, but qualitative analyses should be used in instances where quantitative modeling is not possible**
- **Any mathematical modeling must be done transparently, credibly, and to professional standards by experienced epidemiological modelers and microbial risk assessors**
- **Dynamic compartment models offers an important and insightful analytic approach**
- **Existence of “superspreaders” renders estimates of average effects questionable**

NRC Recommendations (Cont'd): Modeling

- **Uncertainty and sensitivity analyses are mandatory**
- **Community characteristics (e.g. racial, ethnic, and socioeconomic) should be taken into account**
- **Keep in mind that simplicity has advantages**
- **NIH should improve communication with the community about the risk assessment**

BRP Recommendations: Agents for Study

Agents for Study: Key Attributes

- **Intrinsic agent attributes:**
 - Infectivity (primary infection rate, primary routes of human infection)
 - Transmissibility (including secondary and tertiary transmission)
 - Incubation period
 - Infection period
 - Pathogenicity
 - Mortality rate
 - Reservoirs (if known)
 - Vectors (if known)
 - Availability and efficacy of treatments

Agents for Study: Key Attributes

- **Extrinsic attributes:**
 - Relevance to the site locations (actual and alternatives), especially in terms of reservoirs and vectors
 - Extent of epidemiologic data
 - Availability of sound models for a given infectious disease
- **Degree to which an agent is recognized as a public health concern and/or studied at the NEIDL**
 - For example, designation as
 - BSL-3 Agent
 - BSL-4 Agent
 - Category A Agent
 - Select Agent

Recommendation: Comprehensive Range of Agents

- **Agents to be studied should include those that are:**
 - **Highly transmissible, highly pathogenic, and higher case fatality rate**
 - **Highly transmissible, pathogenic, and lower case fatality rate**
 - **Poorly transmissible but highly pathogenic, and higher case fatality rate**
 - **Vector-borne and relevant to the sites to be assessed**

Recommendation: Agents for Study

- Risk assessments should be done for the following agents:

- **1918 pandemic influenza virus**
 - ***Yersinia pestis***
 - ***Francisella tularensis***
 - ***Bacillus anthracis***
 - **SARS-associated coronavirus**
 - **Rift Valley fever virus**
 - **Andes hantavirus**
 - **Junin haemorrhagic fever virus**
 - **Tick-borne encephalitis complex (Russian spring-summer encephalitis) virus**
 - **Lassa fever virus**
 - **Marburg virus**
 - **Ebola virus**
 - **Nipah virus** (*added at the request of BU*)
- BSL 3
- BSL 3 or 4
- BSL 4

NOTE: Agents in **RED** are CDC and/or NIH Category A Agents and/or Select Agents

BRP Recommendations: Scenarios for Study

Recommendation: Scenarios

- **Scenarios should:**
 - **Be scientifically accurate and credible**
 - **Be realistic**
 - **Relate to a real incident if possible**
 - **Include agents that are recognized as a public health concern**
 - **Include releases of infectious agents into the community that are representative of what could occur through:**
 - **Accidental release**
 - **Malevolent action**

Recommendation: “Worst Case” Scenarios

- **State court requested evaluation of “worst case” scenario that involves “risk of contagion arising from accidental or malevolent release of a contagious pathogen.”**
 - **Concept of “worst case”**
 - **Intuitively understood but highly subjective notion**
 - **Therefore “worst case” is a discredited term in the field of risk assessment (e.g., nuclear reactor safety)***
 - **Variations of the scenarios should address underlying concept: “highly unlikely but still credible high consequence event” ***

Type of Scenario	Examples	Sources
Mechanical or Power Failure	Lab Equipment failure	NRC
	Loss of power	Public
	Malfunction of solid and liquid waste disposal systems	Public
Transportation Accident	Transportation Accident	Federal Court, Public
Security Failure	Site security failure	NRC
	Personnel security failure	NRC
Exposure via Fomites or release of Vectors	Fomites bearing transmissible agents	Public
	Vector-borne agent release	NRC, Public
Human Errors	Procedural errors resulting in inadvertent infection (e.g., mislabeled tubes)	NRC, Public
	Infection not diagnosed early and spreads in community, esp. via public transportation	Public
Malevolent Actions	Malevolent actions	NRC, State Court, Public
	Suicide bomber/airplane attack/truck with explosives/fire	Public
	Disgruntled or deranged lab worker spreads agents in community	Public

BRP Recommendations: Methodology and Analyses

Recommendation: Analyses

- **Qualitative analyses:**
 - Should be conducted for all agents and scenarios
- **Quantitative analyses:**
 - Should also be performed in all cases for which sufficient epidemiologic data and validated mathematical models are available
- **Analyses should:**
 - Use proven methods and reflect known epidemiologic data
 - Take into account characteristics of the surrounding community
 - Be transparent regarding any assumptions and sensitivity of analyses

Recommendation: Analyses

- **Analyses should address:**
 - Risk of agent release
 - Probability of occurrence
 - Any uncertainty in critical parameters used
 - For any factor selected for use, the range of published values
 - Available public health interventions
 - Comparative risks at urban, suburban, and rural sites
 - What happens when safety measures and emergency plans do and don't work

Current Status of the Development of the Supplementary Risk Assessment

Current Status

- **Contract awarded in September 2008 and updated in January 2010**
- **The NIH will continue to engage the NRC Committee on Technical Input at key milestones during the development of supplementary risk assessment**
- **Next Steps:** planned approach for the risk assessment will be presented and discussed with communities in Boston

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Questions for Discussion

1. **Is the range of agents being studied appropriate?**
2. **Is the approach to event sequence analysis appropriate?**
 - a. **Will the method result in an adequate range of scenarios being considered and selected for analysis?**
 - b. **Are the plans for analysis and expression of results appropriate?**
3. **Is the modeling approach appropriate?**
 - a. **Is the approach to initial infection sound?**
 - b. **Are the criteria for and selection of models sound?**
 - c. **Are the use of the hybrid branching-compartment models and the extreme values analysis sound?**