II. INTRODUCTION

The National Institutes of Health (NIH) awarded a construction grant on September 30, 2003 to Boston University for the partial funding of the design and construction of one of two National Biocontainment Laboratories (NBLs). These advanced biomedical research laboratories are essential to the civilian biodefense initiative and will provide critically needed Biosafety Level 4 (BSL-4) research space. The basic and translational research to be conducted in these laboratories over the next 20 years will result in development of new diagnostics, vaccines and therapeutics for protection of the American public against intentional misuse or release of harmful biological agents or toxins, and against emerging and re-emerging infectious diseases such as H5N1 influenza ("bird flu") and severe acute respiratory syndrome coronavirus (SARS-CoV).

The NIH completed and published a Final Environmental Impact Statement (FEIS) as required for major federal actions under the National Environmental Policy Act (NEPA) in the Federal Register on December 9, 2005 [70 F.R. 73223-01 (Dec. 9, 2005)]. After public review and comment, a Record of Decision (ROD) was published in the Federal Register on February 2, 2006 [71 F.R. 5670-01 (Feb. 2, 2006)] and construction of the National Emerging Infectious Diseases Laboratory (NEIDL) began at the BioSquare II Research Park on Albany Street, Boston, Massachusetts adjacent to the Boston University Medical Center (BUMC).

During the preparation of the FEIS, the NIH conducted a thorough review of the possible impacts of the NEIDL on the public and the environment. The review demonstrated that the construction and operation of the NEIDL posed a negligible risk to the community in which the laboratory was sited or to the surrounding communities. This assessment also included an analysis of the potential impacts resulting from a hypothetical scenario such as a release of anthrax spores into the surrounding community as a result of an accident in the facility concomitant with a failure of the High Efficiency Particulate Air (HEPA) filters in the exhaust system. This "worst case scenario," which was based on unlikely but plausible events, demonstrated that the risk to the community from a laboratory based accident was essentially zero.

In response to lingering concerns raised by some members of the community with regard to the potential public health risks that could result from a release of exotic infectious agents, the NIH has now performed additional reviews of the possible impacts of the NEIDL. These reviews included additional analyses of alternative sites for construction and operation of the laboratory, as well as risk assessments of potential infectious disease threats that may be posed to the public should an exotic infectious agent be released into the community through an infected laboratory worker, a laboratory accident or other mishap. In response to community arguments that potential public health risks would be lower in less densely populated areas, the risk assessments were conducted for two alternative sites owned by Boston University in Tyngsborough, MA and Peterborough, NH as well as for the BUMC Albany Street site. The first two sites are representative of

suburban and rural locations, respectively. Additionally, the risk assessments specifically addressed an on-going community concern that Environmental Justice (EJ) communities near the proposed NEIDL site in Boston, would be disproportionately impacted in the unlikely event that a release occurred.

The additional site analyses specifically addressed the following:

- Facility Location
- Visual Quality of the Site
- Historic Resources
- Noise Impacts
- Utility Availability and Impacts
- Transportation and Access
- Air Quality Impacts
- Economics, Income and Demographics
- Availability of and Impacts on Healthcare Facilities, Social Assistance and Emergency Response
- Presence of Floodplains
- Wetlands, Riparian Areas and Surface Waters
- Impacts on Habitat, Wildlife and Vegetation
- Impacts on Threatened or Endangered Species
- Impacts on Agriculture and Livestock

The NIH conducted the additional site analyses through site visits, review of public documents and other literature, and interviews.

THE PARTNERS AND THE MODELS

Infectious disease risks and impacts on the three potential NEIDL sites and surrounding communities were investigated through advanced modeling simulations. The NIH engaged the National Center for Geographic Information and Analysis (NCGIA) at the State University of New York (SUNY) at Buffalo, NY, and HealthRx Corporation (Fairfax, VA) to provide advanced modeling and simulation research and services. Consultants in Disease and Injury Control (CDIC, Inc, Atlanta, GA) provided technical and support services. The NIH Division of Environmental Protection (DEP) provided technical expertise and expert advice and guidance during the additional site analyses.

1) SUNY-Buffalo has been prominent in geographic information science research and training since the mid 1970s, and is home to one of the three sites of the NCGIA. The NCGIA is an independent research consortium whose primary mandate is to conduct basic research in geographic information science and related technology. A team of medical, population, social, and transportation geographers and specialists in individual

epidemiologic modeling provided the Agent-based Explicit Spatial and Temporal (**A-BEST**) model to study the potential movement of exotic disease agents, over time and space, through a community.

2) HealthRx Corporation is a medical industry consulting firm specializing in the design and development of software for a wide variety of medical and health-related applications. HealthRx develops highly specialized systems and applications meeting corporate, medical, and government requirements. HealthRx systems are in use around the world and the firm has experience in such diverse areas as preventive and applied medicine, health and fitness, finance and accounting, and law enforcement. HealthRx Corporation developed the Multilayer Agent Based-Simulation Tool (MLAB-ST) Model used to explore potential impacts of vector-borne disease in the three distinct communities (Boston-BUMC; Tyngsborough, MA; and Peterborough, NH) under consideration for siting of the NEIDL.

COMMUNITY INVOLVEMENT

The NIH believed it was critically important that concerned citizens provide input into development of the model and specifically development of the release scenarios to be studied through simulation modeling. To that end, the NIH conducted a series of three public meetings to openly discuss the types of infectious disease agents to be studied and the scenarios through which potential releases could occur. Additionally, an e-mail address and telephone number were established through which citizens could provide comments and suggestions. Through these outreach activities, some citizens suggested the following situations that, in their opinions, could be associated with high-containment laboratories or agents included in the risk assessments.

- A transportation accident with subsequent release of an infectious agent
- A release of a vector-borne disease
- A release of an infected arthropod
- A laboratory incident concerning mislabeling of a specimen or stock culture
- A release of a recombinant organism (**Please Note:** NIH recognizes that rDNA use requiring containment defined as "BL4" by the NIH Guidelines for Research Involving Recombinant DNA Molecules shall not be permitted in the City of Boston. This scenario was added in response to a written comment received from the community)
- A laboratory incident involving Ebola virus
- A laboratory incident involving a poxvirus
- An incident involving a school or school-aged children
- An incident requiring transport of an infected patient

The NIH used both the A-BEST and MLAB-ST modeling approaches (see Section V) to address concerns best summed up by the following public comment: "If public safety is the focus of this new risk assessment, then the assessment cannot be limited to one possible scenario, since there are many scenarios that could result in public danger. Also, true-life complexity cannot be left out of the model for the sake of making the problem tractable. This risk assessment must capture the real world complications in order to have any value in protecting public safety."

DEVELOPMENT OF RISK ASSESSMENT SCENARIOS AND METHODOLOGY

Although the worst case anthrax scenario mentioned above and described fully in the original FEIS showed that a major set of failures would result in no harm to the community, it did not include several aspects of possible events that remained of concern to the community. In order to sufficiently address public concerns, the NIH developed extremely complex, hypothetical scenarios of situations suggested by the public and included the intricate social, work and home interactions and networks of daily life through A-BEST modeling and simulation (See Section VI). Additional modeling was performed for the arthropod-borne disease scenario using the MLAB-ST approach. This model optimized interaction between different agents in the model and tracked expansion of an infected insect population and the impact of the population escalation on disease transmission in a given human population. The scenarios were developed to approximate conditions and outcomes that would, in effect, far overstate the actual risks. The following general approaches were used during development of the hypothetical scenarios.

- Scenarios were highly contrived, although aspects were drawn from past events and the scientific literature where possible.
- Where information was not available, assumptions were made and held constant across the three communities in keeping with the approach to overstate actual risk.
- Scenarios were designed to "force" an infection beyond the laboratory so that the threat to the three communities could be compared. (See Section VII)
- Each laboratory accident or event leading to a simulated infection was given a probability of 1.0 (100%) instead of being subjected to more traditional methods and more realistic probabilities used in the rest of the A-BEST model simulations. (See Section VI)
- Exaggerated probabilities were assigned to events (e.g., Sabia transmission by close contact) in order to force transmission of simulated disease into the three communities.
- No public health interventions (e.g. insect repellents, immunizations, "sharp safe" or needle-free medical devices) were included in the simulations, although this would not be realistic.

In addition to the general approach described above for scenario development, scenario-specific, hypothetical assumptions that far overstated the real risks were applied to each of the four selected diseases to further "force" simulated infection into the communities of Tyngsborough, Peterborough and Boston-BUMC. The purpose of these scenario-specific assumptions was, again, to model hypothetical situations and to ensure that simulated disease did indeed occur at each location so that the impacts on the three distinct communities could be compared.

THE SCENARIOS

As will be discussed in Section IV, the following agents were chosen for inclusion in the risk assessments: Ebola virus; monkeypox; Sabia virus; and Rift Valley Fever virus.

THE REAL RISKS VS. HYPOTHETICAL SCENARIOS

A-BEST modeling was used to most closely simulate real-world interactions and networking, providing millions of interactions and explicit population movement to enhance exposure opportunities. Further, a second modeling technique, MLAB-ST simulation, was used to supplement the A-BEST approach in simulation of vector-borne disease by allowing for free and predictable movement of the vector. In all cases, decisions were made that would, in fact, ***overstate the real disease risks and negative outcomes***. This approach was necessary to ensure that disease would be present in each *simulated* community to allow comparison of *simulated* health impacts, which was the primary goal of the risk assessment. The presence of disease in the communities ***does not represent a real-life situation***; it results from vast over-estimation of the risks for simulation and comparison purposes only.

One example of the over-estimation of risks is the development of the Rift Valley Fever (RVF) scenario for MLAB-ST and A-BEST modeling. MLAB-ST modeling restricted human movement to the modeling communities, a highly unlikely event. Individuals would not leave their community for work, shopping or other social networking, significantly increasing the chance that they would come into contact with an infected mosquito. Mosquitoes (*Aedes canadensis*) were selected as the arthropod vector for the RVF scenarios rather than another biting insect. This was done to increase the risk associated with the simulation because the mosquitoes are not dependent upon a host (e.g., a dog or deer, etc.) for transport or dissemination. They replicate to high levels and they are aggressive biters of humans and livestock. Mosquitoes can transmit the disease vertically as well as horizontally and their eggs survive winter. All of these factors were taken into account in selecting an infectious agent for modeling purposes and in designing a scenario that would ensure establishment of simulated disease in a community solely for computational modeling and comparative purposes.

In A-BEST simulation modeling for RVF, a density of infected mosquitoes was set (10,000 infected mosquitoes per acre of appropriate water habitat), rather than running a scenario with a single or a few infected mosquitoes (which would have been a much more plausible approach), thereby optimizing the transmission of disease into the affected simulated communities. Again, **not a real-life situation** but an attempt to ensure that there were results that could be compared for determination of community impacts.