THE NATIONAL ACADEMIES
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Board on Life Sciences

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November 21, 2007

Ian A. Bowles
Secretary
Executive Office of Energy and Environmental Affairs
100 Cambridge Street, Suite 900
Boston, MA 02114

Dear Secretary Bowles,

At your request, the National Research Council (NRC)[1] established an expert Committee[2] to provide technical input on the document *Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University* (hereafter referred to as the Draft Supplemental Environmental Report, or DSER) to the Executive Office of Energy and Environmental Affairs of the Commonwealth of Massachusetts. The DSER stated that it was prepared by the National Institutes of Health (NIH) in response to concerns raised in a federal court proceeding to address aspects of the construction of a proposed National Biocontainment Laboratory containing a Biosafety Level 4 (BSL-4) facility in the South End of the City of Boston, Massachusetts (the National Emerging Infectious Diseases Laboratory, or NEIDL).

As developed with your office, the Committee's Statement of Task is as follows[3]:

> The Committee will review the NIH Study [Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University] and meet to discuss the methodologies and analyses therein and to address specific questions provided by officials of the Massachusetts Executive Office of Energy and Environmental Affairs. The questions addressed by the Committee will solely pertain to the scientific adequacy of the NIH Study. The specific questions to be addressed are as follows:
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> - Determine if the scientific analyses in NIH Study are sound and credible;
> - Determine whether the proponent has identified representative worst case scenarios;
> - Determine, based on the study's comparison of risk associated with alternative locations,

[1] The principal operating arm of the National Academy of Sciences and the National Academy of Engineering
[2] Committee on Technical Input on the National Institutes of Health's Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University. Committee members and their backgrounds can be found in Attachment A.
[3] The full Statement of Task can be found in Attachment B.

whether there is a greater risk to public health and safety from the location of the facility in one or another proposed location;

The parties acknowledge and agree that the Committee's report will be limited to a technical review of the NIH Study, and the Contractor [NRC] will make no findings or recommendations regarding the adequacy of any determinations or decisions made by any agency or department of the U.S. Government of the State Massachusetts under NEPA [National Environmental Policy Act] or MEPA [Massachusetts Environmental Policy Act], and Contractor shall not be responsible in any way for any such decisions or determinations. The Committee will author a letter report that addresses the foregoing questions and submit this letter report to the Massachusetts Environmental Policy Act Office prior to the end of the public comment period.

Thus, the questions addressed by the Committee will solely pertain to the scientific adequacy of the risk assessment and other analytical methodologies used in the DSER and whether the report responds to the state's questions in a scientifically sound and credible manner. The Committee makes no findings or recommendations regarding the original Risk Assessment and Site Suitability Analysis document *Biosquare Phase II, Boston Massachusetts. Final Project Impact Report/Final Environmental Impact Report (Fort Point Associates, 2004; hereafter referred to as FEIR)* although the Committee refers to the FEIR because it provides a foundation for the DSER. This letter report addresses the foregoing questions and is submitted to you in fulfillment of the contract with the Commonwealth of Massachusetts.

The Committee's answers to the three tasking questions are as follows:

1. Are the scientific analyses in the DSER sound and credible? **Overall, the Committee believes that the DSER as drafted is not sound and credible.**

2. Has the NIH identified representative worst case scenarios? **The DSER as drafted has not adequately identified and thoroughly developed worst case scenarios.**

3. Based on the comparison of risk associated with alternative locations, is there a greater risk to public health and safety from the location of the facility in one or another proposed location? **The DSER does not contain the appropriate level of information to compare the risks associated with alternative locations.**

It is important to recognize that these conclusions are based solely on the Committee's technical review of the DSER, and thus they should not be viewed as statements about the risks of proposed biocontainment facilities in Boston, or in cities more generally. The Committee acknowledges the need for biocontainment laboratories in the United States, including BSL-4 laboratories, and recognizes that BSL-4 facilities are being operated in other major urban areas. The Committee's view is that the selection of sites for high containment laboratories, whether in urban or rural areas, be supported by detailed analyses summarizing the available scientific information.

The Committee provides more detailed answers to the three task questions and recommendations that you and the NIH may wish to consider in the document that follows.

Finally, this report reflects the consensus of the Committee and has been reviewed in accordance with standard NRC review procedures (see Attachment D). This project was funded by the Executive Office of Energy and Environmental Affairs of the Commonwealth of Massachusetts. The work was conducted by staff of the NRC's Board on Life Sciences: Dr. Marilee Shelton-Davenport (study director), Rebecca Walter (program assistant), and Dr. Frances Sharples (Director, Board on Life Sciences).

Sincerely,

John Ahearne, PhD
Chair, Committee on Technical Input on the NIH's Draft Supplementary Risk Assessments And Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University

BACKGROUND AND INTRODUCTION

In 2003, the Boston University Medical Center was awarded a $128 million grant from the National Institutes of Health (NIH) to build one of two National Biocontainment Laboratories. The National Biocontainment Laboratory is designed to support the National Institute of Allergy and Infectious Diseases' biodefense research agenda and will include a Biosafety Level 4 (BSL-4) containment laboratory housed in a 223,000 square foot building. The BSL-4 component of the laboratory is designed to study the most dangerous infectious diseases and pathogens, including hemorrhagic fevers (Ebola, Marburg) and Lassa fever. According to the FEIR (2004), the facility will also house BSL-2 and BSL-3 laboratories.

There are at least five BSL-4 laboratories that are currently operational in the United States. Although the NEIDL BSL-4 laboratory space will account for only 13 percent of the building's total space, it accounts for virtually all of the community concern. The location of the facility on Albany Street in Boston's South End has been extremely controversial and there have been numerous contentious public meetings over the plans for the facility.

The building and BSL-4 laboratory is part of the BioSquare Phase II project. Under the MEPA, the Secretary of the Commonwealth of Massachusetts's Executive Office of Environmental Affairs[4] issued a certificate stating that the BioSquare II project required the preparation of an Environmental Impact Report. In August 2004, the Secretary of Environmental Affairs issued a certificate stating that the FEIR adequately and properly complied with MEPA. This determination was challenged in court, and in July 2006 the Superior Court of Massachusetts vacated Massachusetts' certification of the FEIR and remanded the matter to the Secretary of Environmental Affairs for further administrative action[5]. In response, the Secretary in September 2006 issued a scope for the preparation of a supplemental FEIR (SFEIR) in which the applicant was asked to address a set of additional issues:

- Biocontainment Building: Although the FEIR provided a "worst case" safety analysis involving the loss of the physical integrity of the containment systems using a release of anthrax spores, Massachusetts asked for at least one additional "worst case" scenario analysis arising from an accidental or malevolent release. Smallpox[6], SARS, and Ebola were suggested as potentially representative "worst case" pathogens.

- Alternative sites: Massachusetts asked for analyses of feasible alternative locations for the biocontainment building, including at least one in an area less densely populated than the proposed location in Boston's South End. The supplemental analyses should also evaluate whether the potential public impacts of a pathogen release, including a "worst case" scenario, would be materially different if the biocontainment building were constructed in a feasible alternative location in a less densely populated area.

- Mitigation: Massachusetts asked the applicant to demonstrate that environmental and public health impacts have been avoided to the maximum extent feasible, identify

[4] As of April 11, 2007, organized and named as the Executive Office of Energy and Environmental Affairs.
[5] Ten Residents of Boston v. Boston Redevelopment Authority, No. 05-0109-BLS2, 2006 WL 2440043 (MassSuper.) August 2, 2006.
[6] The Smallpox virus, Variola, could not be used in the Boston facility by international law. This is why the DSER did not address smallpox, although it did address Monkeypox, which may be considered a surrogate for smallpox.

measures to mitigate unavoidable impacts, and identify any appropriate mitigation for impacts that may be identified through the worst case scenarios described above.

The project has also undergone review under the NEPA, and the NIH completed a Final Environmental Impact Statement and issued a Record of Decision in February, 2006. In response to issues raised in a federal court proceeding regarding the NIH Final Environmental Impact Statement, the NIH completed additional reviews of the potential impacts of the BSL-4 laboratory. This report, published by NIH as the *Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University* (hereafter referred to as the Draft Supplemental Environmental Report, or DSER), is designed, in part, to address the state requirement that the SFEIR provide additional worst case scenario analysis and evaluate the comparative levels of risk associated with alternative locations for the BSL-4. Thus, the DSER will form the scientific basis of the SFEIR, which Boston University has not yet filed for state review. The Massachusetts Executive Office of Energy and Environmental Affairs has asked that the Committee evaluate only the DSER, which does not evaluate mitigation. Therefore, the Committee did not directly address the mitigation issue.

In reviewing the DSER, the Committee held an open session on October 19, 2007 in which presentations were made by representatives of the State of Massachusetts, Boston University, NIH, and two scientists identified by opponents of the NEIDL. The list of speakers and their affiliations is in Attachment C. NIH legal counsel determined that the presenting NIH scientist and the scientists contracted to work on the DSER could not answer any questions from the Committee during the open meeting because of restrictions imposed by the NEPA process. Although the NIH did respond in writing to questions submitted by the Committee, the Committee was unable to engage in a meaningful scientific discussion with the scientists contributing to the DSER.

CLARIFICATION OF SCOPE

It is important to note that the Committee was asked to provide only a technical review of the DSER. The Committee did not carry out an independent assessment of the risks associated with the proposed facility or possible alternative locations. The Committee also did not review the FEIR. However, as noted below, the Committee did refer to the FEIR for a definition.

ANSWERS TO CHARGE

1) The Committee was asked to determine if the scientific analyses in the DSER are sound and credible. The Committee used several criteria for judging whether the DSER was "sound and credible". For example,

- Was the investigation framed in such a way that it does indeed constitute an adequate supplementary assessment of the issues raised by the Superior Court of Massachusetts?
- Did the DSER convey information in a transparent fashion so that it is clear how the analyses were conceptualized, constructed, and applied?

- Did the DSER contain sufficient information that the analyses performed could be replicated and confirmed by others?

- Were the assumptions used reasonable and justified by reference to the relevant literature?

- Was the methodology well chosen?

The Committee finds that the DSER is not sound and credible. By this, the Committee means that the conclusions reached in the report are not adequately supported by the analyses nor are they credible for the reasons set out in greater detail below. The Committee is concerned with the pathogens selected for modeling and had numerous reservations about the modeling work and the specifics of the worst case scenarios developed. The Committee also finds a lack of transparency in the DSER, which made evaluating some aspects of the DSER difficult.

2) The Committee was asked to "[d]etermine whether the proponent has identified representative worst case scenarios."

In order to answer this question, the Committee first had to develop a sense of what constitutes a "worst case scenario" given that this term was not specifically defined in the DSER. To explore the meaning of the term worst case scenario, the Committee first consulted the FEIR (2004), which defined worst case scenario according to the maximum possible risk model. This approach uses extreme scenarios that are barely conceivable, but consistent with the environment of risk assessment since the attacks of September 11, 2001.

While this definition provided some information, the Committee did not find it fruitful to identify any particular set of events in developing a sense for the term worst case scenario because as soon as a particular set of events is set, it is usually possible to construct an "even worse" case scenario, generating an escalating chain of situations to evaluate. The Committee thus focused its efforts on preparing relevant questions that would be most useful in analyzing the worst case scenarios set out in the DSER, recognizing that the DSER was intended to be used in decision-making. The Committee viewed the relevant questions as: 1) *Do the scenarios in the document suffice to adequately evaluate the comparative risks to the communities in the DSER?* 2) *Do the scenarios represent those needed to appropriately characterize the risks of the NEIDL?*

Overall, the Committee believes the DSER has not adequately identified and thoroughly developed worst case scenarios in the DSER. The DSER appears to have examined some of the agents identified by the community, but did not effectively examine highly infectious agents that would be of greater relevance to comparing the risks at the three sites. In this and other ways, the DSER did not provide a representative worst case scenario. The DSER also misses the opportunity to present a more refined analysis of the risks presented by a facility like the one under examination and to evaluate comprehensively the impact of a worst case scenario event on public health and safety.

3) The Committee was asked to determine, based on the comparison of risk associated with alternative locations, whether there is a greater risk to public health and safety from the location of the facility in one or another proposed location.

The DSER does examine three sites with different characteristics – inner city, suburban, rural. The Committee endorses the approach of examining sites with different characteristics as a useful aid for decision-making, and endorses the concept of modeling scenarios. Determining whether risks may differ at urban versus rural sites is an important task to assist in decision-making on siting facilities such as the NEIDL.

However, the DSER does not contain the appropriate level of information to compare the risks associated with alternative locations. In judging the information that is presented in the DSER, the Committee expects that the risks of laboratory-acquired infections and releases that would cause infections in the community surrounding the laboratory might be low for all three sites. However, the Committee notes that the conclusions of the DSER are insufficiently supported. Specifically, the Committee lacks confidence that the scenario for Rift Valley Fever Virus (RVFV), the one agent the DSER claims to pose a greater risk to rural populations, was appropriately developed to inform decisions on site selection. To address the question of how risks to public health and safety depend on location, the risk assessment should consider agents with greater transmissibility. In addition, models should produce results consistent with what is known about the impact of population density and address factors such as location of vectors and hosts and the ecology and microenvironment involving vectors and hosts.

The Committee was also dissatisfied with the depth of exploration of public health and safety concerns about environmental justice communities impacted by the alternative site considerations. The DSER does not adequately consider the public health and safety impact of the NEIDL on Boston's South End, an environmental justice community, in comparing the risk associated with alternative locations for the laboratory.

SPECIFIC CONCERNS

The DSER addresses the Boston University Medical Center Albany Street site and two alternative sites, Tyngsborough, Massachusetts and Peterborough, New Hampshire. The DSER contains a comprehensive set of characteristics examined for each site, including zoning and noise (DSER, V-1 to V-164). The consideration of these three sites for the Boston University NEIDL is apparently based on the fact that they are urban, rural and suburban properties owned by Boston University. Further rationale for site selection was not provided, and the Committee did not further address the selection of alternative sites.

The Committee appreciates that the development of the DSER was a challenging task that was undoubtedly subject to substantial time and resource constraints. Unfortunately, the Committee finds serious problems with the DSER. Because a number of the concerns impact the Committee's answers to more than one of the charge questions, they are discussed here by topic rather than by question in the charge. The committee is concerned about the agent selection. However, as described in the modeling section, more than substitution of a new agent is needed. Even with a different agent, similar assumptions without justification about very low transmission, lack of variable number of contacts, and lack of population density-dependence would have the same effect of shutting down human-to-human transmission in any location. In addition to the concerns raised in the body of this document, a list of apparent discrepancies noticed by the Committee is compiled in Attachment E.

Scenarios Described in the DSER

The DSER examined scenarios that begin with the assumption that a release has already occurred. According to the DSER, a consultative process with concerned citizens contributed to the selection of these scenarios. This process involved three public meetings and the establishment of an e-mail address and a telephone number by which citizens could provide further comments and suggestions. The list of possible scenarios generated by this means included:

- 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
- 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 four scenarios examined in the DSER contained many of the elements in this list of public concerns. The Committee commends NIH for taking account of input from concerned citizens in its development of supplemental analyses, but this consultative process apparently led to the selection of agents that did not fully address the issues raised by the Secretary of Environmental Affairs. The NIH selected two BSL-3 agents and two BSL-4 agents (all considered Class A agents by the Centers for Disease Control and Prevention select agent program), set artificial criteria for forcing an infection outside of the laboratory, and developed scenarios based in part on expert opinion and published information about these microbial pathogens (CDC, 2007b).

The chosen scenarios in the DSER are not sufficient to adequately evaluate the comparative risks to the communities, nor are they sufficient to appropriately describe a worst case scenario for the NEIDL. A more suitable analysis would have included the selection of agents that are more transmissible and thus might have created a greater risk of urban outbreaks, as well as an explanation or justification of rationale for the release scenarios.

Selection of Agents

The agents selected were Ebola Hemorrhagic Fever Virus (Ebola), Monkeypox Virus, Sabia Hemorrhagic Fever Virus (Sabia), and Rift Valley Fever Virus (RVFV). The DSER provides inadequate rationale for why these agents were appropriate to describe a worst case scenario or to investigate how risk to public health and safety depends on urban, suburban, or rural location for a biocontainment laboratory. The NEIDL includes the BSL-4 laboratory and lower level BSL-3 laboratories. Agents such as *Yersinia pestis* (pneumonic plague), influenza virus (including virulent strains), SARS virus, and highly pathogenic avian influenza virus are often studied in BSL-3 and other lower-level containment facilities. The selection of agents for the worst case scenario was appropriately not limited to BSL-4 agents as some agents handled in BSL-3 facilities may present more serious potential risks than BSL-4 agents. Agents are

categorized for BSL-4 containment because they cause deadly disease for which there is no treatment, not because they are highly infectious and cause widespread disease.

Both Ebola and Sabia Hemorrhagic Fevers have high mortality rates and require BSL-4 containment. However, Ebola virus is transmissible as a blood-borne pathogen, and experience to date suggests that while theoretically possible, it is extremely unlikely to be spread through the routes of transmission included in the scenario (CDC, 2007a). Thus it is not an agent that is likely to spread widely in any of the communities selected. Sabia virus may be spread by aerosols or droplets, but because very little is known about the epidemiological and clinical aspects of Sabia virus, parameters included in the model had to be based on speculation or extrapolation from other agents. Monkeypox requires BSL-3 containment. Monkeypox is spread by contact, with the opportunity to be transmitted from certain small mammals, such as gerbils (referred to in the DSER as "pocket pets"). RVFV, a zoonotic agent that is primarily a disease of ruminant animals, is handled in a BSL-3 facility and is easily transmissible through mosquito vectors.

Selected Agents Should Have Higher Transmission Probabilities

The DSER would have been more useful in supporting decision-making had it considered candidate infectious agents that have the potential to lead to large infection rates in an exposed human population. The three scenarios involving directly transmitted diseases (Ebola Hemorrhagic Fever, Monkeypox and Sabia Hemorrhagic Fever) each dealt with infections characterized by low probabilities of person-to-person transmission (i.e., those infections with a basic reproduction ratio (R_0) that approaches or is actually below one) and thus could not lead to a major epidemic or community outbreak. The final epidemic sizes that were generated by the model for these three scenarios were so small that it is unlikely that differences between Boston, Tyngsborough, and Peterborough could have been detected even if they did exist. A worst case scenario should include an agent with a higher person-to-person transmission rate, represented by a basic reproduction number (R_0) greater than one. A complete scenario could also consider transmission via aerosol droplets and/or fomites (inanimate objects). Diseases should also include those with different latent and infectious periods. These factors will affect the number of subsequent infections, as well as the opportunity for timely response or treatment during an outbreak or epidemic.

A Vector-Borne Agent with More Likely Urban Reservoirs Should Have Been Selected

The vector-borne agent selected was dependent on a ruminant reservoir, which could have been anticipated to generate minimal risk in an urban setting. There are vector-borne diseases with more likely urban reservoirs, and these should be considered. For example, diseases with characteristics of dengue hemorrhagic fever virus, if dengue-competent mosquitoes are found in the site areas. See also the section on vector selection in the Other Considerations section below.

Novel Pathogens

The potential for accidents involving novel or poorly characterized pathogens was not considered in the DSER.

Selection of Release Events

Each of the scenarios in the DSER starts with an assumption that an index case occurs, to ensure subsequent introduction of the pathogen agents to the community. This introduction includes causation by accident and subsequent contacts in family and community settings. The assessment included stakeholder-suggested release scenarios, but this may not have captured an appropriate range of anticipated worst case scenarios. The DSER provides no rationale for why the release scenarios were appropriate to describe "worst cases".

It would be useful to include an analysis of documented probabilities (qualitatively if not quantitatively) of occurrence for several categories of events such as:

- Equipment failure (e.g., containment failure due to maintenance, power outages, or other issues)
- Site personnel security failure
- Procedures (inadvertent infection of one or more laboratory staff)
- Malevolent action

Such data would be useful in selecting the biological agents, operating conditions, and circumstances to generate an appropriate range of release scenarios and their consequences for evaluation.

A base of literature describing the incidence of laboratory-acquired infections[7] does exist (Sulkin and Pike, 1951a; Sulkin and Pike 1951b; Collins and Kennedy, 1999; Harding and Byers, 2006; Sewell, 1995). Although laboratory-acquired infections may be underreported, the data should be considered in a risk assessment framework. Statements like "so low as to be essentially zero" related to laboratory-acquired infections in a BSL-4 environment are not supported by systematic quantitative or qualitative risk assessments in the DSER[8]. It would be more useful to limit the statements to a description of BSL-4 safety history, or to characterize the known rate of laboratory worker infection in the U.S. and Canadian BSL-4 operations as "less than one in X operating hours", or "less than one in X facility-years". In addition, while it is fair for the DSER to point to and rely to some degree on the record of BSL-4 laboratories when considering the likelihood of non-malevolent infection, the safety records of BSL-3 laboratories would also be instructive.

Again, the DSER scenarios all begin with a single infected individual or, in the case of Sabia, a small number of infected lab workers. While such incidents are possible, there are other ways to initiate infection and disease, such as inadvertent laboratory release or malevolent action. These other modes of release can have far more serious consequences than those modeled in the DSER. In addition, malevolent actions were not explicitly discussed in the scenarios examined in the DSER. Even if malevolent action is improbable, an appropriate range of malevolent action scenarios should be considered in the selection of credible worst case events.

[7] The cited Rotz document focuses on qualitative attributes of bioterrorism agents, not the incidence of laboratory-acquired infections. The references cited above provide information about laboratory-acquired infections.
[8] See also discussion about comments like this in the risk communication section below.

Concerns About The Modeling

Modeling is a useful approach to describe worst case scenarios and in this case to compare scenarios among sites. With respect to the modeling work in the DSER, the Committee had a number of concerns. Some of these concerns stemmed from what was described about the modeling and others stemmed from a lack of transparency about the input data, assumptions, and how the model worked.

Insufficient Description of Model Architecture

The one paragraph statement on page VIII-16 of the DSER, which describes the development and architecture of the model, falls short of adequately describing the assumptions contained in the model and their impacts on model predictions. At a minimum, a fuller description of the model architecture is needed so that the work in the DSER can be replicated and evaluated.

The A-BEST Model and Multilayer Agent Based-Simulation Tool (MLAB-ST) seem too basic for modeling a mosquito-borne disease such as RVF. It was not apparent that the model developers had considered, or were familiar with, the epidemiology of mosquito-borne diseases. The DSER has a section on validation (page VIII-15), but the models did not appear to have been appropriately validated by comparing them to other disease models in the literature on insect-borne and other infectious diseases.

Outcome May Not Have Been Sufficiently Influenced by Important Biological Factors

Most importantly, the Committee was concerned that the model did not appear to recognize biological complexities and reflect what is known about disease outbreaks and other biological parameters. The Committee was also uncomfortable with the notion that an attempt to include "true-life complexity" in and of itself increases the value of a model. The DSER dwelt in great detail on the geographical data sets used to generate the synthetic populations that were the basis of the simulations, but the DSER did not explain adequately why this complexity improved the modeling exercise with respect to the questions being asked. More importantly, the DSER used only simplistic methods to deal with biological factors. As explained below, the Committee believes that the modeling would have benefited by recognizing other complexities, including population characteristics and different contact patterns and opportunities. In these areas, epidemiologic and public health data could have been useful for adding relevant conditions associated with life complexity.

Transmissibility can depend on population density, presence of susceptible human subpopulations, characteristics of microenvironments (residences, areas where people are in close physical contact, such as on a bus or subway car), ecology of vectors (mosquitoes, other insects) and hosts (cows, rodents, others), and the interdependence of microenvironments and ecological systems on the geographic characteristics. Selecting the appropriate scope and assumptions for analysis will depend on the characteristics of the disease agent.

The DSER states as a conclusion that only for the RVF scenario is there a difference in risk among the three locations: "The key to the generation of a RVF outbreak is the obligatory presence of flood conditions and large numbers of mosquitoes. Both of these conditions exist in Tyngsborough and Peterborough and the added presence of amplification hosts boosts the risk of disease outbreak even higher" (DSER, VIII-16). The rationale is that in this scenario, mosquitoes act as the vector and more mosquitoes (and ruminants such as bovine hosts for the

disease) are found in the rural and suburban areas than at the Albany Street inner city location. As qualitative reasoning, this may seem plausible. However, the extensive calculations made by the models do not add significantly because it is not clear that the models incorporate the details important for representing how the disease transmission process would develop in the three alternative locations. Details that are important, such as persistence of water bodies where the relevant strains of mosquitoes can reproduce, were not presented in enough detail for the Committee to review them.

Data Quality and Need for Uncertainty and Sensitivity Analyses

The DSER was insufficient in its discussion of the quality and representativeness of the data that were used to inform the choice of model parameter values. In particular, the statement that "true-life complexity cannot be left out of the model" (DSER, II-4) can be challenged in light of the failure to acknowledge the simplicity with which the model represented the natural history of disease transmission. The analyses would be more convincing if the biological rationale were provided for the choices made about parameters and the impact of these choices had been explored with uncertainty and sensitivity analyses.

The Committee was concerned that the DSER did not provide such analyses—two different and well-established techniques for analyzing the strengths and limitations of both general and microbial risk assessments (Morgan and Henrion 1990; Codex Alimentarius Commission, 1994; Burmaster and Anderson 1994; Nauta 2000). Together, uncertainty and sensitivity analyses help distinguish the effects on model outcomes of a lack of knowledge in estimating input parameters and how sensitive outcomes are to changes in modeling assumptions. The lack of an uncertainty analysis makes it difficult to identify the level of knowledge about the parameters used in setting up the scenarios and modeling. A listing of the input parameters, the source of the information used to estimate them, an evaluation of the quality and consistency of the evidence supporting the parameters, and an analysis of the general magnitude and direction of error if the values are wrong are expected and core components of uncertainty analyses in current risk assessment practice. Sensitivity analyses demonstrate how model predictions change with changes in the values of key parameters and can document and transparently convey how assumptions about parameter values influence the variability of results. Uncertainty and sensitivity analyses can communicate confidence in the credibility of the model based on available data and assumptions. They are especially important in situations like this where there is uncertainty in parameter values measured in small published studies. It is also especially important to explain the results of these analyses to stakeholders. Concern by stakeholders may lessen with more careful attention to depicting realistic scenarios and the impact of assumptions for uncertain parameter values on model predictions. Assumptions that were questioned by the Committee elsewhere in the report, and new model parameters suggested by the Committee, should be subjected to sensitivity analyses especially when solid data to support the assumptions are not available.

While the parameter values describing the probability of transmission given particular kinds of contact (e.g., casual contact; household contact; contact with infectious blood or body fluids, including sexual contact; contact between patients and health care workers) appear to be reasonable[9] except as noted in other areas of this report, a sensitivity analysis would reveal the effect of variations in transmission rates. This analysis is critical because the reason that risks

[9] The Committee did not confirm the values, but they did not appear inconsistent with the Committee's knowledge.

appear low for RVFV and for the other three agents is that low values were used for transmissibility (i.e., secondary transmission). Because the probability of transmission of disease from one person to another was set to be low, infections die out, rather than propagate. As a result, for all four of the agents considered, the risks calculated from the two models are small.

Sensitivity of Model to Population Density

Population size and density are important aspects of the differences between sites that can affect the epidemiology of infectious disease. A comparison of risk must, therefore, take into account population differences between urban and rural sites in modeling infectious diseases known to behave differently in such different settings. The model results as presented in the DSER, however, do not seem to be sensitive to population density. The model predicted quite low and similar attack rates (the fraction of a population infected in an epidemic) for the Ebola, Sabia, and Monkeypox scenarios in the different locations despite population density differences. This may indicate that population density was not properly accounted for in the model, but could also be due to other factors, including the possibility that the model was not calibrated with the appropriate transmissibility levels for the various infectious agents studied. Although the model was shown to behave as expected with parameters that are not pathogen-specific, the Committee could not find in the published literature (Bian and Liebner, 2007) a validation of this model with pathogen-specific parameters. Neither was there a comparison with the well-established models that identify differences among cities of different sizes (Rohani et al., 1999) or with agent-based models developed to evaluate the effects of interventions on specific infectious diseases (Eubank et al., 2004; Halloran et al., 2002). Is the model used in the DSER consistent with these published results? Does it accurately reproduce the course of annual influenza infections, or periodic outbreaks of measles? What are the sensitive parameters that must be changed to allow for an epidemic in the absence of medical intervention? There is no evidence presented that this model allows for the possibility of epidemics, even though it claims to not include public health interventions. Although scientists may not know how the analyzed agents will behave in US populations, there are multiple pathogens that can cause epidemics on a regular basis (e.g., influenza, tuberculosis, gonococcus, meningococcus, HIV, Methicillin-resistant Staphylococcus aureus). There are many more that can cause epidemics unless well-established interventions (vaccination, patient isolation, treatment) are employed. A basic validation of this model would include demonstrating that it accurately predicts the course of these well-described epidemics.

Concerns about Model Input, Stated Assumptions and Technical Issues

Although the details of the workings of the model are not sufficiently described, some of the stated assumptions appear to dictate outcomes that undermine the ability to distinguish between locations.

Lack of Public Health Interventions

Many of the parameter values used in the model were estimated based on situations in which public health interventions were in place. In contrast, the modeling was described as assuming that no public health interventions were in place. While the assumption of no public health interventions is described as conservative, this conservatism does not affect all scenarios equally, undermining site comparisons. For example, it may unfairly bias the rural location in the case of no interventions to deal with mosquitoes.

Lack of Host Heterogeneity Modeling

The Committee recognizes that an agent-based model was used to satisfy public concerns that "true life complexity cannot be left out of the model just to make the model tractable", but it is not clear that the advantages of agent-based models were exploited in this DSER. Such models are particularly good at revealing the influence of heterogeneities in the host population. Examples of host heterogeneity that might matter in this instance—especially with respect to comparing consequences of a release for each of the populations at the three sites—include host characteristics that may affect susceptibility and case fatality rates. But there was no reference to expected or plausible differences in transmission probability for those at special risk (the very young, the very old, those with preexisting conditions, and those with compromised immune systems). Also see discussion about environmental justice factors below.

Secondary Transmission Rate

Monkeypox is assumed to have a secondary transmission rate (from the first infected human to the second) of 8.3% based on cited data of 8.3 transmission events per 100 contacts over an 11 year period in the Congo. Although the DSER refers to documentation of six successive human-to-human transmissions in natural infection settings, the modelers inexplicably decrease the tertiary transmission rate (second or subsequent infected human to the next) to 0.03%. The 276-fold rate reduction between the first human to human transmission and the second is not supported by citations, and predetermines that when the model is run 200 times there will be, on average, no chain of more than three transmissions at any location.

Contact Rate and Travel

Travel to and from the facility is assumed in the DSER to be by privately operated vehicle for all three locations. One important difference between a small town and a large city is the number of contacts that each individual may have on an average day. This is both intuitive and substantiated by multiple modeling efforts and contact tracing studies. However, the DSER appears to have made the assumption, not clearly described or justified, that each person has ten contacts (per day?) regardless of the population density of the location: While difficult for the Committee to assess because of insufficient detail, the description of "a full mix pattern at homes and a partial mix with an average of ten contacts at work places and service places" seems to suggest that in work places and service places, at least, the contact rate was somehow fixed at ten and not determined by the network structure. This assumption about the number of contacts further reduces the opportunity for transmission and effectively eliminates one of the most important differences between locations. In such a case, population density may well have had no influence on model outcome.

The Committee also questions the assumption that use of public transportation (trains or buses) is unlikely in the case of the South End of Boston inner city location. The Committee suggests that there may be a higher potential for aerosol transmission of disease in such crowded microenvironments where aerosol transmission between humans may be very important as a mechanism for the spread of contagious diseases (Nicas and Sun, 2006; Bridges et al., 2003; Tellier, 2006).

Possible Oversight of Ruminant Populations

The fourth scenario involved a vector borne infection (RVFV) whose dependence on large water bodies and a ruminant reservoir is well documented. The modelers chose to populate

the suburban and rural locations with one ruminant species (cattle) whose density was determined from the recent USDA AgCensus. No cattle were allocated to the urban location.

The resulting RVFV simulations projected large differences among the attack-rates in each of three host populations. This is not surprising given the assumed respective differences in the presence of water bodies and ruminant populations. The DSER goes on to say that the "data clearly demonstrate that without an amplification host present in the community upon which multiple mosquitoes can feed, RVFV will not be sustained and human infection will not occur". However, RVFV is often associated with small ruminant populations, and there is no evidence that the DSER investigated the possibility that small ruminants are sold in urban live animal markets in Boston. Such markets exist in many other large North American cities (New York, Philadelphia, San Francisco) and often cater to minority ethnic communities.

Number of Model Simulation Repetitions

A purely technical issue is the number of model simulations. The model results were apparently derived from only 200 simulations for each scenario. The DSER does not provide evidence substantiating whether 200 repetitions were enough to stabilize the model. It is not uncommon for single scenarios in agent-based models to require more than a thousand repetitions before clear patterns emerge.

Incomplete Exercise of Risk Analysis Methodology

Ideally, this type of assessment would present information consistent with established quantitative microbial risk assessment (QMRA) methodology (e.g., Codex Alimentarius Commission, 1999; ILSI, 2000) and principles of good practice for risk assessment (e.g., Burmaster and Anderson, 1994; Morgan and Henrion, 1990). Rotz (2002), which was referenced by the DSER as a source of information for agent selection, categorized biological agents by level of civilian threat, but these categorizations alone are not definitive as measures of risk given attendant uncertainties.

A comprehensive QMRA would inform stakeholders about the complexity of biological interactions in pathogenesis and disease transmission that complicate the ability to predict the probability of primary infection and secondary transmission (although primary infection in the DSER was assumed to occur). For example, there is a body of literature that describes increasing likelihood and severity of disease with increasing "dose" of pathogen/microbe exposure—i.e., dose-response relationships (Bieber, et al., 1998; Collins and Reploge, 1997; Glynn and Bradley, 1992; Pickering et al., 2004). The FEIR cited some examples from this literature for inhalation anthrax dose-response data and models, but the DSER lacked a parallel discussion and synthesis of available data (and models) for the supplemental agents. Presentation of dose-response assessment is needed for the supplemental agents selected in order for the DSER to meet the standards of QMRA and principles of good practice for risk analysis in general (Burmaster and Anderson, 1994; Morgan and Henrion, 1990). Variability should also be discussed for each aspect of the disease triangle (host, pathogen, environment, and interactions).

Information on Ebola virus illustrates why QMRA is important (Leroy et al., 2000; Warfield et al., 2004; Geisbert et al., 2003). The literature suggests that innate host immunity causes asymptomatic infection by the Ebola virus and suggests thresholds of resistance for healthy immunocompetent individuals, even without additional barriers to infection in BSL

laboratories. Also, knowledge of the underlying mechanisms controlling the initial events of disease progression exists in animal and human hosts.

Other Considerations in Site Comparisons

The Committee perceives that there are a number of other potential issues regarding dependence of public health and safety impacts on the sites that are not adequately explored in the DSER. Several of these issues are described here.

Health Considerations of Environmental Justice Communities

Environmental justice issues are both exposure modifiers (probability of infection depends on location microenvironment and synergistic exposure to other stressors) and effect modifiers (probability and severity of adverse health consequences are increased by poorer baseline health condition and poorer access to good medical treatment). Issues of how inner city environmental justice communities differ from communities in other locations need further exploration in the DSER. Environmental justice communities are often faced with environmental stressors that wealthier communities do not face. The Committee was dissatisfied with the depth of exploration of such issues in the DSER. In the case of the South End of Boston community, stressors could include the following issues.

Health Status

The DSER did not consider the health status of the population surrounding the prospective facility. For example, the prevalence of asthma, immunosuppressive diseases, and poor nutrition in the environmental justice community, in comparison to the Tyngsborough and Peterborough communities, may be expected to worsen disease morbidity and spread in the event of a biological agent release from the facility. Again, a sensitivity analysis of the model would help guide how these conditions could be useful in assessing population risk.

Public Health

In comparing the locations, the DSER also did not adequately consider public health issues, including access to medical care and health services, of the communities surrounding the facility. For example, while the neighborhood surrounding the Boston location is close to excellent area hospitals, proximity alone is not sufficient to identify, characterize and halt a potential outbreak.

In the event that members of a community are infected by the release of a transmissible biological agent release from the facility, it will be important to detect and contain the disease as quickly as possible to stop the chain of infection. The degree to which sophisticated acute care facilities are needed to identify cases should be considered along with lack of, or marginal access to, public health services, which is typical of environmental justice communities such as the Boston community (Northridge et al., 2003; Krieger et al., 2005; Kayman and Ablorh-Odjidja, 2006; CDC, 2005). Inadequate access to health services and incomplete disease surveillance could hamper the ability of health professionals to detect an outbreak, especially if disease symptoms are largely non-specific during the time that the disease is transmissible.

Vector Selection

The worst case scenarios did not consider the presence of relevant disease vectors in the environmental justice community, such as insects and rodents. The worst case scenario chosen to consider vector spread of disease in the DSER only highlighted the potential dangers of cows as reservoirs in a rural community.

OBSERVATIONS ON RISK COMMUNICATION

In its charge, the Committee was asked to discuss the methodologies and analysis in the DSER and address three specific questions posed by the Commonwealth of Massachusetts. As part of this review of methodologies, the Committee considered the risk communication aspects of the DSER. Several Committee members are individuals experienced in risk communication, and the Committee is compelled to comment on several aspects of communication that could be improved by following risk communication criteria outlined in several National Research Council (NRC) reports (e.g., *Improving Risk Communication*, NRC, 1989; *Understanding Risk: Improving Decisions in a Democratic Society*, NRC, 1996) and other resources.

Particularly in the case of strong public interest, including this siting decision, it is important to develop presentations and documents that are transparent, complete, and clearly address the concerns of interested and affected parties. As explained in the Committee's review, the DSER's methodology and analysis is not transparent, is not complete, and may not address the fundamental concerns of the community, particularly regarding environmental justice.

In light of this inadequacy, statements in the DSER that the risks are "negligible" and "vastly overstated" can appear unfounded and dismissive of public concerns.

ATTACHMENT A: BIOGRAPHICAL SKETCHES OF COMMITTEE MEMBERS

John Ahearne (chair) is Executive Director Emeritus of Sigma Xi, the Scientific Research Society, and Emeritus Director of the Sigma Xi Ethics Program. Prior to working at Sigma Xi, Dr. Ahearne served as Vice President and Senior Fellow at Resources for the Future and as Commissioner and Chair of the U.S. Nuclear Regulatory Commission. He worked in the White House Energy Office and as Deputy Assistant Secretary of Energy. He also worked on weapons systems analysis, force structure, and personnel policy as Deputy and Principal Deputy Assistant Secretary of Defense. Serving in the U.S. Air Force (USAF), he worked on nuclear weapons effects and taught at the USAF Academy. Dr. Ahearne's research interests include risk analysis, risk communication, energy analysis, reactor safety, radioactive waste, nuclear weapons, materials disposition, science policy, and environmental management. He was elected to the National Academy of Engineering in 1996 for his leadership in energy policy and the safety and regulation of nuclear power. Dr. Ahearne has served on many NRC Committees in the past twenty years, and has chaired a number of these, including the current Committee on Evaluation of Quantification of Margins and Uncertainty Methodology Applied to the Certification of the Nation's Nuclear Weapons Stockpile and the Committee on the Internationalization of the Civil Nuclear Fuel Cycle. In 1966, Dr. Ahearne earned his PhD in Physics from Princeton University.

Thomas W. Armstrong is Senior Scientific Associate in the Exposure Sciences Section of ExxonMobil Biomedical Sciences, Inc., where he has been working since 1989. Dr. Armstrong is also working with the University of Colorado Health Sciences Center as the lead investigator on exposure assessment for epidemiological investigations of potentially benzene-related hematopoietic diseases in Shanghai, China. Dr. Armstrong also spent nine years working for the Linde Group, as both the manager of loss control in the gases division and as a manager of safety and industrial hygiene. Dr. Armstrong recently conducted research on quantitative risk assessment models for inhalation exposure to Legionella. He is currently a member of both the Society for Risk Analysis and The American Industrial Hygiene Association, and he has been certified as an Industrial Hygienist by the American Board of Industrial Hygiene. Dr. Armstrong has an MS in Environmental Health and a PhD in Environmental Engineering from Drexel University.

Gerardo Chowell is an Assistant Professor at the School of Human Evolution and Social Change at Arizona State University. Prior to joining ASU, Dr. Chowell was a Director's postdoctoral fellow with the Mathematical Modeling and Analysis group (Theoretical Division) at the Los Alamos National Laboratory. He performs mathematical modeling of emergent and re-emergent infectious diseases (including SARS, influenza, Ebola, and Foot-and-Mouth Disease) with an emphasis in quantifying the effects of public health interventions. His research interests include agent-based modeling, model validation, and social network analysis. Dr. Chowell received his PhD in Biometry from Cornell University and his engineering degree in telematics from the Universidad de Colima, Mexico.

Margaret E. Coleman is a Senior Microbiologist at Syracuse Research Corporation (SRC) in the Environmental Science Center, an independent not-for-profit research and development organization. Ms. Coleman leads multi-disciplinary teams in SRC's Microbial Risk Assessment Center of Excellence (M-RACE) and is a founding member and councilor of the new Upstate

NY Society for Risk Analysis (SRA) chapter. From 1996 to present, she served in various leadership roles in SRA: chair of symposia and workshops in quantitative microbial risk assessment (QMRA); program committee member for domestic and international conferences; and offices in the Biostressors Specialty Group and Dose-Response Specialty Group. Also an active member of the American Society for Microbiology (ASM), she recently contributed an article to ASM's Microbe magazine (*Microbial Risk Assessment Scenarios, Causality, and Uncertainty*). Ms. Coleman contributes to peer review processes in QMRA for several journals, including SRA's journal *Risk Analysis*. She served as a reviewer for the NRC Report *Reopening Public Facilities After a Biological Attack* and as a committee member on the *Review of Testing and Evaluation Methodology for Biological Point Detectors*. Prior to her work in SRC, Ms. Coleman contributed to development of QMRA methodology for foodborne and waterborne hazards at USDA and with member agencies of the federal Risk Assessment Consortium. Ms. Coleman earned her BS degree from SUNY College of Environmental Science and Forestry at Syracuse and MS degrees from Utah State University and the University of Georgia in Biology/Biochemistry and Medical Microbiology.

Gigi Kwik Gronvall is a Senior Associate at the Center for Biosecurity of University of Pittsburgh Medical Center (UPMC) and Assistant Professor of Medicine at the University of Pittsburgh. An immunologist by training, Dr. Gronvall's work addresses how scientists can diminish the threat of biological weapons and how they can contribute to an effective response against a biological weapon or a natural epidemic. She is a term member of the Council on Foreign Relations and also serves on the American Association for the Advancement of Science (AAAS) Committee on Scientific Freedom and Responsibility. Dr. Gronvall is a founding member of the Center for Biosecurity of UPMC and, prior to joining the faculty in 2003, she worked at the Johns Hopkins University Center for Civilian Biodefense Strategies. From 2000-2001 she was a National Research Council Postdoctoral Associate at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in Fort Detrick, Maryland. Dr. Gronvall earned a PhD from Johns Hopkins University for her work on T cell receptor/MHC I interactions.

Eric Harvill is an Associate Professor of Microbiology and Infectious Diseases at the Pennsylvania State University. His primary research interest is in the interactions between bacterial pathogens and the host immune system, and his group investigates both bacterial virulence factors and host immune functions at the molecular level using the tools of bacterial genetics and mouse molecular immunology. These studies investigate the effects these molecular-level activities may have on the population-level behavior of infectious diseases. Dr. Harvill has served on several NRC committees, including the Committee on Methodological Improvements to the Department of Homeland Security's Biological Agent Risk Analysis. He has reviewed for more than 20 scientific journals and serves on the Editorial Board for *Infection and Immunity*. Dr. Harvill has reviewed proposals for six different NIH study sections, the USDA and multiple international funding organizations. He has organized international and local meetings and chaired sessions at annual meetings of both the American Association of Immunologists and the American Society for Microbiology. He earned his PhD at the University of California, Los Angeles.

Barbara Johnson, PhD, RBP has over 15 years of experience in the U.S. government in the area of biosafety, biocontainment and biosecurity, and currently owns the consulting company Barbara Johnson & Associates, LLC. Dr. Johnson has managed the design, construction and commissioning of a BSL-3 Aerosol Pathogen Test Facility, and she launched the U.S. government's first chemical and biological counterterrorism training facility. Research areas include biological risk assessment and mitigation, testing the efficiency of respiratory protective devices, and testing novel decontamination methods against biological threat agents. In the private sector she pioneered the development of the first joint biosafety and biosecurity programs between the U.S. and institutes in the former Soviet Union, and founded and directed a Center for Biosecurity in association with this work. She has served as the President of the American Biological Safety Association, and is the Co-editor of the journal Applied Biosafety.

Paul A. Locke is an Associate Professor in the Department of Environmental Health Sciences at the Johns Hopkins Bloomberg School of Public Health. He is a public health scientist and attorney with expertise in risk assessment and risk management, radiation protection law and policy, and alternatives to animals in biomedical testing. Dr. Locke serves on the Environmental Protection Agency's Clean Air Act Advisory Committee and is a member of the Board of Councilors of the National Council on Radiation Protection and Measurements. In 2004 he was appointed to, and remains a member of, the NRC Nuclear and Radiation Study Board, and has participated on two NRC Committees that evaluated the risks associated with the disposal of high level radioactive waste. Dr. Locke has received several awards, including the Yale School of Public Health Alumni Service Award, and the American Public Health Association Environment Section Distinguished Service Award. He holds an MPH from Yale University School of Medicine, a JD from Vanderbilt University School of Law, and a DrPH from the Johns Hopkins Bloomberg School of Public Health.

Warner North is President of NorthWorks, Inc., a consulting firm in Belmont, California. Dr. North is also a consulting professor in the Department of Management Science and Engineering at Stanford University. Over the past thirty years, Dr. North has carried out applications of decision analysis and risk analysis for electric utilities in the U.S. and Mexico, for petroleum and chemical industries, and for government agencies with responsibility for energy and environmental protection. He has served as a member and consultant to the Science Advisory Board of the Environmental Protection Agency since 1978, and as a Presidentially appointed member of the U.S. Nuclear Waste Technical Review Board. Dr. North currently serves as a member on the NRC's Panel on Public Participation in Environmental Assessment and Decision Making and has chaired NRC Committees. Dr. North is a past president of the International Society for Risk Analysis, a recipient of the Frank P. Ramsey Medal from the Decision Analysis Society for lifetime contributions to the field of decision analysis, and a recipient of the Outstanding Risk Practitioner Award from the Society for Risk Analysis.

Jonathan Richmond is CEO of Jonathan Richmond and Associates, a biosafety consulting firm with a global clientele. Prior to starting his own firm, Dr. Richmond was the director of the Office of Health and Safety at the Centers for Disease Control and Prevention in Atlanta, Georgia. He is an international authority on biosafety and laboratory containment design. Dr. Richmond was trained as a geneticist, worked for ten years as a research virologist, and has been involved in the field of biosafety for the past 25 years. He has authored many scientific

publications in microbiology, chaired many national symposia, edited numerous books, and is an international consultant to ministries of health on laboratory safety and training. He served as President of the American Biological Safety Association.

Gary Smith is Chief of the Section of Epidemiology and Public Health in the School of Veterinary Medicine at University of Pennsylvania. He has a secondary appointment in the Department of Biostatistics and Epidemiology at Penn's School of Medicine and is an Associate Scholar in the Center for Clinical Epidemiology and Biostatistics. He is also an affiliated faculty member of Penn's Institute for Strategic Threat Analysis and Response. His research deals with the epidemiology and population dynamics of infectious disease in humans as well as wild and domestic animal species. He has extensive experience of mathematical modeling in the context of infectious and parasitic disease control strategies (including the evolution of drug resistance) and has published case-control studies on a range of infectious diseases of animals and humans. Dr. Smith served on an FAO/WHO Expert Committee on the implementation of farm models in the developing world; he served on the Pennsylvania Food Quality Assurance Committee, and he was a member of a European Union Expert Committee on Bovine Spongiform Encephalopathy risk. He has served on the editorial boards of Parasitology Today, The International Journal of Parasitology, The Veterinary Quarterly, and Frontiers in Ecology and the Environment. Dr. Smith earned Bachelors degrees in Zoology and Education from the Universities of Oxford and Cambridge respectively and a D.Phil in Ecology from the University of York.

ATTACHMENT B: STATEMENT OF TASK

The Committee will review the NIH Study [Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University] and meet to discuss the methodologies and analyses therein and to address specific questions provided by officials of the Massachusetts Executive Office of Energy and Environmental Affairs. The questions addressed by the Committee will solely pertain to the scientific adequacy of the NIH Study. The specific questions to be addressed are as follows:

- Determine if the scientific analyses in NIH Study are sound and credible;
- Determine whether the proponent has identified representative worst case scenarios;
- Determine, based on the study's comparison of risk associated with alternative locations, whether there is a greater risk to public health and safety from the location of the facility in one or another proposed location;

The parties acknowledge and agree that the Committee's report will be limited to a technical review of the NIH Study, and the Contractor [NRC] will make no findings or recommendations regarding the adequacy of any determinations or decisions made by any agency or department of the U.S. Government of the State Massachusetts under NEPA or MEPA, and Contractor shall not be responsible in any way for any such decisions or determinations. The committee will author a letter report that addresses the foregoing questions and submit this letter report to the Massachusetts Environmental Policy Act Office prior to the end of the public comment period.

ATTACHMENT C: ACKNOWLEDGEMENTS

The chair thanks the Committee for working extremely hard on a very tight schedule to produce this report and for their willingness to adjust personal schedules to convene in Washington, DC on short notice. He also thanks Rebecca Walter for handling the complicated logistics required for the Committee to be successful and notes the most valuable contribution was made by the study director, Dr. Marilee Shelton-Davenport, whose knowledge and patient leadership was instrumental in producing a quality report.

The Committee also thanks those who participated in the open session October 19, 2007 (Attachment C) and those who submitted comments and documents to the Committee in writing.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We thank the following individuals for their review of this report:

John Applegate, Indiana University
John Bailar, The National Academies
Kenneth Berns, University of Florida Genetics Institute
David Franz, Midwest Research Institute
Charles Haas, Drexel University
Marc Lipsitch, Harvard University
Stephen Ostroff, Pennsylvania Department of Health
Peter Palese, Mount Sinai School of Medicine
Bailus Walker, Howard University
Catherine Wilhelmsen, The United States Army Medical Research Institute for Infectious Diseases

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Ed Perrin, University of Washington, and John Samet, Johns Hopkins University. Appointed by the National Research Council, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring Committee and the institution.

ATTACHMENT D: OCTOBER 19, 2007 OPEN SESSION PUBLIC AGENDA

Technical Input on the NIH's Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University

Friday, October 19, 2007

Keck Room 101, 500 Fifth Street, NW
Washington, DC 20901

8:30	**Presentation of Charge by Sponsor** *Deerin Babb-Brott* *Assistant Secretary for Environmental Impact Review, Executive Office of Energy and Environmental Affairs, Commonwealth of Massachusetts*
9:00	**NIH Comments** *Deborah E. Wilson, Dr. P.H.* *Director, Division of Occupational Health and Safety, ORS, NIH*
9:45	**Boston University Comments** *Mark S. Klempner, M.D.* *Associate Provost for Research* *Boston University Medical Campus* *Director, National Emerging Infectious Diseases Laboratories Institute*
10:15	**Questions for Boston University**
10:45	*Break*
11:00	**Stakeholder Representative Comments** *David Ozonoff, MD, MPH (by telephone/ videoconference)* *Professor of Environmental Health, Chair Emeritus, Department of Environmental Health* *Boston University School of Public Health*
11:30	**Stakeholder Representative Comments** *Marc Lipsitch, PhD* *Professor of Epidemiology* *Harvard School of Public Health*
12:00	**Questions for stakeholders**
12:45	End of open session

ATTACHMENT E: LIKELY DISCREPANCIES

The Committee believes that undertaking to simulate scenarios for four additional agents at three proposed sites was very ambitious given the time constraints for this project. There is internal evidence that the section on modeling was hurriedly assembled (including numerous typographical errors, apparently contradictory statements, abbreviated and incomprehensible summaries of data from the literature, references to "influenza" which were not analyzed, and the discussion of parameter values that appear to refer to pathogens not considered in the four scenarios). Some examples of errors include:

- On page VI-10, the DSER states as an assumption that "0.9% of individuals will develop hemorrhagic disease [attributable to Rift Valley Fever] of whom 50 % will die. 0.003% fatality rate for the remaining infected individuals." Yet in the "rationale for inclusion" of Rift Valley Fever on Page IV-20 it is stated that a recent outbreak of this disease has "caused at least 1065 confirmed human cases and 315 deaths". No attempt is made to reconcile or explain this discrepancy or why the lower dose fatality rate was selected for use in the Rift Valley Fever scenario.

- On page VI-24, the biting rate of *Aedes Canadensis*, "an aggressive biter", was recorded as ">260 bites per minute". Is this a typographical error?

- On page VI 19, the model flow for the MLAB-ST model contains the statement that "If there is a ruminant present it gets bitten [and] if the mosquito is infectious the virus is transmitted to the ruminant. By contrast, on page VI-25, it is assumed that the "mosquito-ruminant infectivity is 21% at 7 days and 15% at 14 days".

- Page VI-16 contains the sentence, "If they survive, the individual obtains life long immunity, except for influenza because new strains may be introduced". An influenza outbreak is not one of the depicted scenarios. On the same page, it is stated that "An infection rate of 0.1 is used for adults and a rate of 0.15 is used for children and seniors". Again, this seems to apply to influenza and not any of the selected scenarios.

ATTACHMENT F: REFERENCES

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