Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas

Committee on the Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas

Board on Life Sciences
Board on Agriculture and Natural Resources
Division on Earth and Life Studies

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COMMITTEE ON THE EVALUATION OF A SITE-SPECIFIC RISK ASSESSMENT FOR THE DEPARTMENT OF HOMELAND SECURITY'S PLANNED NATIONAL BIO- AND AGRO-DEFENSE FACILITY IN MANHATTAN, KANSAS

RONALD M. ATLAS (*Chair*), Professor of Biology and Public Health and Co-director, Center for Health Preparedness, University of Louisville, Louisville, KY

THOMAS W. ARMSTRONG, Principal Investigator, TWA8HR Occupational Hygiene Consulting, LLC, Branchburg, NJ

MICHAEL S. ASCHER, Visiting Researcher, University of California, Davis, CA

MARK T. HERNANDEZ, Professor of Environmental Engineering, University of Colorado at Boulder, Boulder, CO

BARBARA JOHNSON, Consultant for Biosafety and Biosecurity, Johnson & Associates, LLC, Herndon, VA

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E. Paul Gibbs, *University of Florida*
Philip Hagan, *Georgetown University*
Peter B. Jahrling, *National Institute for Allergy and Infectious Diseases*
Roger Kasperson, *Clark University*
William W. Laegreid, *University of Illinois at Urbana-Champaign*
Jonathan Richmond, *Jonathan Richmond & Associates*
Joseph Scire, *Atmospheric Studies Group, TRC*
Gary Smith, *University of Pennsylvania*
Alan Washburn, *Naval Postgraduate School (Emeritus)*
Ronald H. White, *Johns Hopkins Bloomberg School of Public Health*
Alex Winter-Nelson¸ *University of Illinois at Urbana-Champaign*

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 **Corrie Brown**, *University of Georgia*, and **Lynn Goldman**, *George Washington 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.[1] Responsibility for the final content of this report rests with the author committee and the institution.

[1]After the prepublication version of the report was provided to the sponsor for a required security review, the committee provided a few modifications in the text to clarify statements that may be misconstrued.

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ACRONYMS AND ABBREVIATIONS

BMBL – Biosafety in Microbiological and Biomedical Laboratories
BRI – Biosecurity Research Institute
BSE – bovine spongiform encephalopathy
BSL – biosafety level

CDC – Centers for Disease Control and Prevention
CEEZAD – Center of Excellence for Emerging and Zoonotic Animal Diseases (DHS)

DADS – Davis Animal Disease Simulation
DHS – Department of Homeland Security

EIS – environmental impact statement

FAD – foreign animal disease
FADD – foreign animal disease diagnostician
FMD – foot-and-mouth disease
FMDv – foot-and-mouth disease virus

GAO – Government Accountability Office

HAN – Health Alert Network
HEPA – high-efficiency particulate air
HSPD-9 – Homeland Security Presidential Directive 9, "Defense of United States Agriculture and Food"
HVAC – heating, ventilating, and air conditioning

IAQ – indoor air quality
ID – infectious dose

KSU – Kansas State University

MRHC – Mercy Regional Health Center

NAADSM – North American Animal Disease Spread Model
NAHLN – National Animal Health Laboratory Network
NBAF – Nation Bio- and Agro-Defense Facility
NCMI – National Center for Medical Intelligence
NIH – National Institutes of Health
NOAA – National Oceanic and Atmospheric Administration
NorthCom – U.S. Northern Command
NVS – National Veterinary Stockpile

NWS – National Weather Service

OIE – Organisation Mondiale de la Santé Animale (World Organisation for Animal Health)

PCR – polymerase chain reaction
PFU – plaque-forming units
PIADC – Plum Island Animal Disease Center

RVF – Rift Valley fever
RVFV – Rift Valley fever virus

SCIPUFF – second-order closure integrated puff model
SME – subject matter experts
SPC – Storm Prediction Center
SSRA – site-specific risk assessment

TRA – threat risk assessment

USAMRIID – U.S. Army Medical Research Institute for Infectious Diseases
USDA – U.S. Department of Agriculture
UTMB – University of Texas Medical Branch

WTP – willingness to pay

THE NATIONAL ACADEMIES
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Board on Life Sciences
Board on Agriculture and Natural Resources

500 Fifth Street, NW
Washington, DC 20001
Phone: 202 334 2215
Fax: 202 334 1289
E-mail: bls@nas.edu

November 1, 2010

The Honorable Tara O'Toole, M.D., M.P.H.
Under Secretary for Science and Technology
U.S. Department of Homeland Security
Washington, DC 20528

Dear Dr. O'Toole:

At the request of the U.S. Congress and the Department of Homeland Security (DHS), the National Research Council's Division on Earth and Life Studies established the ad hoc Committee on the Evaluation of a Site-Specific Risk Assessment (SSRA) for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas. The SSRA is extremely important for understanding the risks posed by and the potential effects of placing the NBAF in Manhattan, Kansas. It provides critical guidance for design and operation of the facility to ensure that risk can be reduced through appropriate design, training, and operational procedures; effects can also be reduced through surveillance and mitigation planning. The involvement of this committee is an important component of this critical activity. The committee examined the SSRA work plans and specific questions posed by DHS so that it could advise DHS about the approach to the SSRA. DHS completed the SSRA in late June 2010. In July and August 2010, DHS supplied additional written responses to the committee's questions about the SSRA. All page references in this report are to the June 2010 version of the SSRA and the follow-up materials provided in July and August, which were submitted to the committee for its evaluation. Because of the time constraints imposed by Congress, the SSRA and its evaluation turned out to be a heroic effort, on the part of both DHS and the committee. A great deal of work was accomplished in a very short time.

As chair of the committee, I wish to thank the NRC staff, the committee members, and DHS for their responsiveness to the demands of generating the SSRA and its review within the required time. This has been an interactive and iterative process aimed at producing the best estimates of risk and of potential effects associated with construction of the NBAF in Manhattan, Kansas. This final report constitutes the committee's evaluation of the SSRA.

Sincerely,

Ronald M. Atlas, *Chair*
COMMITTEE ON THE EVALUATION OF A SITE-SPECIFIC RISK ASSESSMENT FOR THE DEPARTMENT OF HOMELAND SECURITY'S PLANNED NATIONAL BIO- AND AGRO-DEFENSE FACILITY IN MANHATTAN, KANSAS

Summary

The Department of Homeland Security (DHS) is preparing to build the National Bio- and Agro-Defense Facility (NBAF), a new state-of-the-art high-containment facility that will replace the aging Plum Island Animal Disease Center and will serve as a linchpin in protecting U.S. agriculture from foreign animal disease threats. DHS selected Manhattan, Kansas, as the site for the new NBAF after a site-selection process that involved an environmental impact statement to model the potential spread of foot-and-mouth disease (FMD), one of the most serious foreign animal disease threats, and a threat risk assessment (TRA) to estimate security risks associated with sites under consideration. The Government Accountability Office (GAO) had raised concerns about DHS's analysis and methods. Hearing those concerns, Congress instructed DHS to complete a site-specific biosafety and biosecurity risk assessment (SSRA) of the proposed NBAF facility in Manhattan, Kansas, before construction funds would be obligated. The legislation (P.L. 111-83, see Box 1-1) also directed the National Research Council to conduct an independent evaluation of the SSRA to determine its adequacy and validity (see Box 1-2 for the Statement of Task).

The National Research Council convened a multidisciplinary committee of experts (see Appendix A for committee biosketches) to provide DHS with feedback on its initial work plan and to evaluate the adequacy and validity of the final SSRA. In March 2010, the committee issued a privileged preliminary letter report to provide DHS with guidance on its proposed approach for conducting the SSRA; DHS accepted most of the committee's recommendations and revised its work plan accordingly. In June 2010, the completed SSRA was delivered to the committee for review. During July and August 2010, DHS supplemented the SSRA with responses to questions and concerns from the committee.

Assembling the data and performing the SSRA of NBAF was a large undertaking; therefore DHS and its contractors should be commended for performing the SSRA within a remarkably short time frame. This final report constitutes the committee's evaluation of DHS's SSRA.

OVERALL ASSESSMENT

The committee evaluated the SSRA's methods, facility design plans, and mitigation strategies. The committee found that the models used in performing the SSRA appear to be appropriate and that many of the SSRA's general conclusions are valid. The SSRA has considered the major release pathways (aerosols, fomites, liquid waste, and solid waste), as recommended in the committee's preliminary letter report (see Appendix B), and has addressed mitigation strategies for each. DHS has also appropriately responded to GAO's prior criticism that it had inappropriately dealt with a potential plume from an airborne release of foot-and-mouth disease virus (FMDv); the SSRA uses a state-of-the-art puff dispersion model to simulate the aerosol transport of pathogens, which turned out to be a less critical pathway of FMDv spread than the near-site exposure of cattle. However, as described in the findings below, the

committee found that the SSRA had several major shortcomings with respect to potential risks and impact scenarios, and there are some critical limitations in the SSRA's execution and analysis.

The committee found that the SSRA has many legitimate conclusions, but the SSRA is not entirely adequate or valid. The SSRA does not account for the overall risks associated with operating the NBAF and conducting FMDv work in Manhattan, Kansas. The inputs and assumptions for the models are inadequate because they do not fully account for how a biosafety level 3 agriculture (BSL-3Ag) and BSL-4 facility would operate, how pathogens might be released, and which animal populations might be exposed. The SSRA sometimes used arbitrary assumptions and did not account for uncertainties, some of which require experimental data that are currently not available but that could greatly alter the outputs. Consequently, the committee is concerned about the validity of the actual risk and impact levels determined by the SSRA's outcomes from the models.

Given more time, the SSRA may have progressed further and may have better addressed some of the concerns expressed in this report. The committee thus views this as a notable first step in an iterative process aimed at identifying and minimizing risk and determining actions that will need to be taken.

FINDINGS

The SSRA shows that constructing the NBAF in Manhattan, Kansas, carries a number of risks and that the impact of an FMDv release could potentially have significant economic, health, and national security impacts. Some risks and impacts are generic to any high-containment large-animal facility, whereas others are specific to the Manhattan, Kansas, site. The risk of release is primarily a generic concern, whereas the risk of infection, spread, and impact is largely related to the site. The SSRA's estimates indicate that the probability of an infection resulting from a laboratory release of FMDv from the NBAF in Manhattan, Kansas approaches 70% over 50 years (see Figure 3-1) with an economic impact of $9-50 billion. The committee finds that the risks and costs could well be significantly higher than that, and elaborates on those findings below.

Finding 1: The SSRA lacks evidence to support the conclusion that the risk of release that results in infection is very low relative to the risk of infection introduced from an external source.

The SSRA states that "given the combination of proven biocontainment design and robust operation procedures and response planning, the NBAF operations in Manhattan, Kansas overall brings extremely low risk relative to the greater risk of the intentional or accidental introduction of FMDv by an external source" (page 1, SSRA follow-up letter, July 28, 2010). Although the committee affirms that engineering and operational safeguards can substantially lower the risk of release, the committee does not concur with the implied conclusion of the SSRA that there is a very low risk of release that would result in an infection. That comparison "to the risk of intentional or accidental introduction" is misleading because the SSRA does not consider or quantify the risk of infection from an external source; thus, with no data for comparison, the SSRA's conclusion of "extremely low risk" is invalid.

Furthermore, the SSRA's characterization of risk as very low is inconsistent with the risk of infection presented in the SSRA's estimates over the expected lifetime of the NBAF. The SSRA did not account for the cumulative risk of a release and infection that could spread across the expected life span of the NBAF. Assuming that the SSRA risk estimates are credible and reliable, if the risk probabilities across all escape pathways and scenarios had been taken into account, the SSRA would have indicated that an escape of a pathogen, such as FMDv, and an ensuing disease outbreak is more likely than not to occur within the 50-year life span of the NBAF. As previously mentioned, the SSRA's estimates indicate that a release of FMDv resulting in infection outside the laboratory has a nearly 70% chance of occurring with an economic impact of $9-50 billion. Also, because the SSRA did not account for important uncertainties and risk factors as discussed below, the SSRA could well have underestimated the risk of pathogen release and transmission and its consequences. In many scenarios considered, the numbers probably represent conservative estimates of risk.

Finding 2: The SSRA overlooks some critical issues, both site-specific and non-site-specific, that could significantly elevate the risk of accidental release and spread of pathogens.

While the SSRA considered site-specific characteristics that affect risk— including the area's high risk of tornadoes and it being in the vicinity of a transportation hub for cattle and other livestock—it neglected to consider the risks associated with the NBAF's proximity to a metropolitan area and other animal facilities. This includes exposure and fomite risks for Kansas State University (KSU) and its football stadium (which would potentially expose a large human population), its College of Veterinary Medicine (where sick and susceptible animals are treated and where there are large numbers of transient animal patients), and other research facilities (and movement of personnel between KSU, the Biosecurity Research Institute, and the NBAF). In addition, the SSRA neglected to consider the maintenance and cleaning of BSL-3Ag and BSL-4 large animal pens, which would result in aerosol formation of pathogens and emissions much greater than were assumed in the aerosol scenario in the SSRA. The cleaning scenario is likely to lead to significantly increased risks of infection through fomites and airborne pathways.

Finding 3: The SSRA has several methodological flaws related to dispersion modeling, tornado assessment, and epidemiological modeling. Thus the committee believes that questions remain about the validity of the overall risk estimates.

A common flaw in the execution of the dispersion, tornado, and epidemiological models was that many of the assumptions used for the model parameters were arbitrary and subject to user bias. Although sensitivity analyses were conducted, these did not systematically address many important uncertainties and risks related to release, transmission, and mitigation. Many scenarios were potentially overoptimistic, and could well have led to major underestimations of the risks. Specifically, the committee could not determine the input parameters used for the NAADSM and could not independently validate the results.

Finding 4: The committee agrees with the SSRA's conclusion that for FMDv, long-distance plume transport will likely be less important than the near-site exposure of cattle.

Near-site exposure of cattle and other livestock are especially a concern in Kansas State University's College of Veterinary Medicine, sales barns, and the many cow-calf operations and feedlots within a few miles of the NBAF; beef cattle sales barns are a particular focal point for secondary transmission of FMDv in this setting. These livestock and their transport across neighboring states will serve as major factors in the spread and amplification of an FMD outbreak throughout the United States. As shown in the SSRA, the high level of animal movement and the presence of sales barns near Manhattan, Kansas, significantly increase the degree of FMD spread and its economic impact.

Finding 5: Substantial gaps in knowledge make predicting the course of an FMD outbreak very difficult, which led to weaknesses in the SSRA.

Predictions of epidemic size are only as robust as the weakest links in the model, and the SSRA identified a lack of good records and data on interstate livestock transport. Without data, there is no way to fill in the gaps and improve precision beyond the scope of expert opinion. In addition, without improvements in data quality, it remains difficult to obtain any robust forecasts of overall outbreak effects. Even though specific data are lacking for predicting the nature and scope of SSRA escape scenarios, data are available on recent FMDv introductions or laboratory escapes and they provide valuable lessons in understanding realistic expectations for mitigation measures and disaster preparation plans for various outbreak scenarios.

Finding 6: Although the economic modeling was conducted with appropriate methods, the epidemiological estimates used as inputs to the SSRA were flawed.

The epidemiological modeling assumptions that were used in the economic assessment, such as depopulation rates and outbreak duration, were overoptimistic in their estimates. The committee questions the SSRA's assumption that its proposed mitigation strategy would contain the spread of FMD by culling 120-720 herds per day (page 230 of the SSRA). The committee does not think that infected herds could be detected and culled at that rate, and therefore questions the validity of the mitigation strategy to limit the effects of an outbreak. If fewer herds could be culled each day, the spread and impact would be much higher than indicated by the SSRA. Consequently, the use of flawed epidemiological inputs resulted in economic estimates that were also flawed and invalid, albeit derived in a methodologically sound manner.

Finding 7: The committee agrees with the SSRA's conclusion that early detection and rapid response can limit the impact of an FMDv release from the NBAF, but is concerned that the SSRA does not describe how the NBAF could rapidly detect such a release.

Early detection is critical for limiting the spread of infection, therefore it will be important to develop extensive real-time surveillance for FMDv and other pathogens being worked on at the NBAF before the laboratory becomes operational. Surveillance will also be critical in detecting whether a leak or spill has occurred within the NBAF so that steps can be taken to minimize and mitigate its release. To implement FMD surveillance and response in the United States, numerous capabilities will need to be developed related to real-time diagnostics,

real-time full-genome surveillance, a real-time active surveillance system, and response plans with appropriate parties involved in FMD diagnosis, control, and eradication.

Finding 8: The SSRA lacks a comprehensive mitigation strategy developed with stakeholder input for addressing major issues related to a pathogen release. The mitigation strategies that are provided do not realistically demonstrate current or foreseen capacity for how federal, state, and local authorities would effectively respond to and control a pathogen release.

With regard to human health and the NBAF's site in Manhattan, Kansas, the committee is concerned about the lack of clinical isolation facilities and world-class infectious disease clinicians experienced in diagnosing and treating laboratory staff or communities exposed to BSL-4 pathogens. With regard to animal health, the SSRA acknowledges that the Manhattan, Kansas, region is a hub of animal movement for the entire United States and that infected animals would be expected to move across the country and cause pockets of infection at great distances from the initial source of infection, but the mitigation strategies do not address outbreaks of such magnitude. Given that a pathogen release from the NBAF may occur despite all efforts to prevent that from occurring, it will be necessary to create realistic and credible mitigation strategies for the release of a pathogen.

Finding 9: The committee agrees with the SSRA's conclusion that human error will be the most likely cause of an accidental pathogen release, and fomite carriage is the most likely way that a pathogen would escape the facility's outer biocontainment and biosecurity envelope.

Safe practices are of paramount importance given that the SSRA presents human error as the most likely source of accidental releases. To enhance safe operation and reduce the risk of human error identified in the SSRA, the committee agrees that key NBAF personnel will need adequate ongoing training, education, and evaluation of skills. Furthermore, there will need to be zero tolerance of deviations from biosafety standards and practices recommended by the CDC and USDA.

Finding 10: The committee agrees with the SSRA's conclusion that investment in biosafety and biosecurity engineering and the training of personnel and responders can reduce the risks, but is concerned about current design plans that potentially compromise safety measures.

The NBAF will venture into a new and unprecedented area of BSL laboratory operations with respect to its mainland location, scale of operations, and scope of agents. Given that the SSRA states that the cost of a release (such as a release of FMDv) would be very high, the facility will need to be engineered beyond the accepted standards to an exceptionally high level of biosafety and biosecurity. To function safely, it will need to be a state-of-the-art facility with state-of-the-art equipment and state-of-the-art biosafety practices. It would be prudent not only to abide by the strongly recommended guidelines set forth in the most recent *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, but to also glean best practices and guidance from existing BSL-4 laboratories. The committee is seriously concerned about the

SSRA's current designs which omit redundant HEPA filters—but are strongly recommended by the *BMBL*—for reasons of practicality and cost-savings. Any facility design compromises due to budgetary limitations will need to be viewed as inconsistent with the mission of providing a state-of-the-art facility with minimal risk of pathogen escape from containment. The critical engineering and construction plans will affect the containment potential for the life span of the facility. Once construction of the NBAF is complete regardless of the location, funding will need to be maintained to assure continued safe operation and maintenance.

Finding 11: The SSRA's qualitative risk assessment of work with BSL-4 pathogens in large animals was inadequate.

The qualitative risk assessment was inadequate because it failed to fully consider the characteristics of the pathogens and the risks of working with BSL-4 pathogens in large animal facilities. The committee does not concur with the SSRA's finding that its quantitative risk assessment regarding FMDv and Rift Valley fever virus (RVFV) sufficiently represents the range of risk regarding the other pathogens that will be studied at the NBAF, that is, the pathogens that are included in the qualitative risk assessment. The committee does not agree that the BSL-3 quantitative risk assessment adequately frames the risks associated with operating a BSL-4 large animal facility, because it is insufficient to use BSL-3 pathogens to predict risks associated with BSL-4 pathogens that are zoonotic and for which no treatment is available. Given that the qualitative risk assessment was inadequate and that the SSRA did not perform a quantitative risk assessment for BSL-4 agents, further evaluation of risks and mitigation strategies will need to be established for BSL-4 agents (for example, Nipah and Hendra viruses or other emerging BSL-4 zoonotic pathogens) to identify ways of minimizing the risks associated with working with those agents in a large animal facility setting.

ADDITIONAL REMARKS

The SSRA team should be applauded for its effort in conducting an extensive risk assessment in such a short period of time. Although the committee's findings express major concerns about the validity of some of the SSRA's conclusions, the work that was completed constitutes a huge step forward compared with previous risk assessments of its kind and should be viewed as a solid starting point.

The nation clearly needs an institution to support comprehensive research programs for the study of foreign animal and zoonotic diseases, including detection, diagnosis, and means of mitigation (drugs, vaccines, and genomic forensics). Such activities require a capability to work with all known threat agents (not just the eight infectious agents listed in the SSRA), multiple pathogen introductions, and emerging and unknown disease threats. For these reasons, the committee agrees that there is a need for a facility like the NBAF to be constructed and operated in the United States.

Constructing a BSL-3Ag and BSL-4 facility of the magnitude planned for the NBAF, one that is capable of large animal work on a scale greater than other high-containment laboratories, undoubtedly presents new and unknown risks that could not be accounted for in the SSRA because of a lack of data and experience. Given the constraints of the design framework and the short timeframe available for data collection and analysis, the committee finds that the

limitations of the data, facility design details, and operating practices may have limited the scope that the SSRA could adequately address at this time. As more data, facility designs, and operational plans emerge, updated analyses may be appropriate to better evaluate the risks posed by a BSL-3Ag and BSL-4 large animal facility in Manhattan, Kansas.

The SSRA and the committee identify some sources of risk that can be addressed as part of the design, preparation, and long-term operation of the NBAF to reduce risk wherever it is located. Though the SSRA and the committee offer several points for consideration to reduce the risk of a pathogen release and its consequences, further risk analysis is needed to determine the extent to which these measures would reduce risk. Ultimately, policymakers will need to decide whether the risks are acceptable related to constructing and operating the NBAF in Manhattan, Kansas, and DHS will need to determine steps to minimize risk and impact if construction and operation should proceed as planned.

1

Introduction

BACKGROUND

In its 2002 report *Countering Agricultural Bioterrorism: The Role of Science and Technology*, a National Research Council (NRC) committee identified gaps in knowledge about foreign animal disease pathogens that reduced the reliability and timeliness of risk-assessment and risk-management decisions, and it determined that the ability to detect and identify some animal pathogens rapidly after introduction was inadequate (NRC, 2002). After the creation of the Department of Homeland Security (DHS), that issue was partly addressed by Homeland Security Presidential Directive 9 (HSPD-9), *Defense of United States Agriculture and Food*, which directs the Secretary of Agriculture and the Secretary of Homeland Security to "develop a plan to provide safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases." To meet its obligations under HSPD-9, DHS plans to construct and operate a new facility: the National Bio- and Agro-Defense Facility (NBAF).

The planned NBAF is envisioned as a state-of-the-art high-containment facility that will support programs that the nation and others will turn to as a global reference, training, and research laboratory for foreign animal diseases.[1] The improved facility will replace the aging Plum Island Animal Disease Center (PIADC) and will enable DHS and the U.S. Department of Agriculture to fulfill their critical missions of conducting basic and applied research in diagnostics, detection, vaccine development, and training. The NBAF will differ from other high-containment laboratories in that it will have the potential to carry out critical research on agents that pose serious threats to U.S. animal and human health by using large animals (such as cattle and swine) and will presumably lead in developing effective vaccines, therapeutics, and diagnostics for animal diseases, including genomics related to threat agents and zoonotic diseases. [2] It will also provide critical diagnostic capacity for identifying emerging foreign

[1]A foreign animal disease is an animal disease caused by an agent that does not occur naturally in the United States. The disease is limited to agricultural animals (NRC, 2005).

[2]A zoonotic disease or infection is transmissible between animals and humans, and is caused by a bacterial, viral, parasitic, or unconventional agent. Zoonoses are a public health concern. Many zoonoses also affect animal health and thus prevent the efficient production of food animals and create obstacles to international trade in animals and animal products (WHO, 2008; IOM and NRC, 2009).

animal and zoonotic diseases and unknown threats. Thus, the NBAF will be an important asset in securing the economy, human and animal health, and the security of the nation, in addition to assessing potential threat agents, for decades to come.

DHS began a site-selection process for the NBAF in January 2006. As part of its evaluation, DHS prepared an environmental impact statement (EIS) to model the potential extent of dispersal of foot-and-mouth disease virus (FMDv) and prepared a threat risk assessment (TRA) to estimate security risks for the six sites under consideration (DHS, 2008). In January 2009, DHS selected Manhattan, Kansas, as the site for the new NBAF (Federal Register, 2009). The Government Accountability Office (GAO) raised concerns about DHS's analysis of the risks related to performing FMDv research on the mainland, faulted the EIS's choice of a Gaussian plume model, and found DHS's economic analysis flawed in that the EIS did not address domestic market impacts of an FMD outbreak (GAO, 2008, 2009). As a result of the differing views of DHS and GAO about the adequacy of the studies used in the selection of Manhattan, Kansas, as the site for the NBAF, the FY 2010 DHS Appropriation Act (P.L. 111-83) instructed DHS to complete a site-specific biosafety and biosecurity mitigation risk assessment (SSRA) associated with the proposed facility "which includes an integrated set of analyses using plume modeling and epidemiological impact modeling to determine the requirements necessary to ensure safe operation of the NBAF at the approved Manhattan, Kansas, site" (see Box 1-1). The legislation also directed DHS to work with the NRC to conduct an independent evaluation of the SSRA (see Statement of Task in Box 1-2) and prohibited the obligation of funds for NBAF construction before completion of the review.

Box 1-1
Public Law 111-83: Department of Homeland Security Appropriations Act, 2010

Sec. 560. (a) None of the funds made available by this Act may be obligated for construction of the National Bio- and Agro-defense Facility on the United States mainland until 30 days after the later of:

(1) the date on which the Secretary of Homeland Security submits to the Committee on Appropriations of the Senate and the House of Representatives a site-specific bio-safety and bio-security mitigation risk assessment, which includes an integrated set of analyses using plume modeling and epidemiologic impact modeling, to determine the requirements necessary to ensure safe operation of the National Bio- and Agro-defense Facility at the approved Manhattan, Kansas, site identified in the January 16, 2009, record of decision published in Federal Register Vol. 74, Number 11, and the results of the National Academy of Sciences' review of the risk assessment as described in paragraph (b): Provided, That the integrated set of analyses is to determine the extent of the dispersion of the foot-and-mouth virus following a potential laboratory spill, the potential spread of foot-and-mouth disease in the surrounding susceptible animal population, and its economic impact: Provided further, That the integrated set of analyses should also take into account specific local, State, and national risk mitigation strategies; or

(2) the date on which the Secretary of Homeland Security, in coordination with the Secretary of Agriculture, submits to the Committees on Appropriations of the Senate and the House of Representatives a report that:

(A) describes the procedure that will be used to issue the permit to conduct foot-and-mouth disease live virus research under section 7524 of the Food, Conservation, and Energy Act of 2008 (21 U.S.C. 113a note; Public Law 110-246); and
(B) includes plans to establish an emergency response plan with city, regional, and State officials in the event of an accidental release of foot-and-mouth disease or another hazardous pathogen.
(b) With regard to the integrated set of analyses included in the mitigation risk assessment required under paragraph (a)(1), the Secretary of Homeland Security shall enter into a contract with the National Academy of Sciences to evaluate the mitigation risk assessment required by subsection (a)(1) of this section and to submit a Letter Report: Provided, That such contract shall be entered into within 90 days from the date of enactment of this Act, and the National Academy of Sciences shall complete its assessment and submit its Letter Report within four months after the date the Department of Homeland Security concludes the risk assessment.

Box 1-2
Statement of Task

In reaction to criticism from the Government Accountability Office (GAO), the FY 2010 DHS Appropriation Act (P.L. 111-83) prohibits the obligation of funds for construction of the new National Bio- and Agro-Defense Facility (NBAF) until the Secretary of Homeland Security undertakes a site-specific biosafety and biosecurity mitigation risk assessment for the Manhattan, Kansas site. Once DHS completes the risk assessment, the Congressional language mandates that the National Academy of Sciences provide an independent evaluation of the DHS analyses. Therefore, under the auspices of the Board on Life Sciences and the Board on Agriculture and Natural Resources, the National Research Council (NRC) will convene a committee of experts to review the DHS site-specific risk assessment. The committee will not perform an independent evaluation of the safety of the NBAF, but will restrict its findings to assessing the adequacy and validity of the site-specific risk assessment.

DHS is currently conducting a source selection process for a contractor to manage the development of the risk assessment. Subsequent to the selection, the committee will undertake its first task to answer questions related to the selected contractor's work plan brought to it by DHS. In this capacity, prior to the contractor beginning their modeling and risk assessment process early in 2010, the NRC Risk Assessment Committee will meet with DHS in order to review the contractor's Work Plan for the Risk Assessment and answer questions from DHS related to the plan. The NRC Risk Assessment Committee will convene to review the contractor's Work Plan and the questions provided by DHS and will provide a brief letter report to DHS in response to these questions within four weeks of this meeting. This brief letter report will not be available to the public until the second letter report of the NRC Risk Assessment Committee is available to the public. Following the delivery of the final Risk Assessment report by the performer to DHS, the committee will undertake its second task to review the finished site-specific risk assessment and prepare a second and final letter report containing its findings within four months of receiving the performer's report from DHS.

COMMITTEE'S APPROACH TO ITS TASK

The National Research Council convened a committee of experts (see biosketches in Appendix A) to evaluate the SSRA of the planned NBAF in Manhattan, Kansas. In preparation for the SSRA, DHS submitted a draft work plan for the committee to review and 28 written questions for the committee to address. The draft work plan provided a general overview of the proposed methods and models that DHS and its contractors would use to conduct the SSRA.

Preliminary Work Plan Advice

The committee issued a preliminary letter report (see Appendix B) that reviewed the SSRA draft work plan, answered the 28 specific questions, and provided recommendations on how to improve the work plan. In considering the draft work plan, the committee recognized that the NBAF's new location and new capabilities would introduce a new set of risks. The committee felt that the SSRA would have to account for site-specific biosafety and biosecurity mitigation strategies in addition to risk assessment. The committee believed that in planning for the NBAF and preparing for its eventual operation, the SSRA would need to inform about the potential risks of pathogen escape so that plans could be appropriately developed to reduce risk (such as modifications in facility engineering design and operation plans) and mitigate potential consequences.

DHS initially proposed a narrow interpretation of the congressional mandate for an SSRA that would have focused almost exclusively on foot-and-mouth disease virus (FMDv) and plume modeling of an aerosol release. DHS revised the work plan to include risks posed by Rift Valley fever virus on the basis of discussions with the committee on February 25, 2010 (see Appendix C for meeting agendas). After reviewing the preliminary SSRA work plan, the committee recommended a much broader approach that would consider other agents and risks relevant to the NBAF, including zoonotic agents (FMDv rarely infects humans and is not a public health threat) and other infectious agents that may require biosafety level 4 (BSL-4)[3] containment (FMDv is a BSL-3 agent[4]); the committee also recommended that other routes of release be considered (such as release via fomites, liquid waste, and solid waste) because recent cases have shown these routes to be major pathways of FMDv escape from laboratories (see Appendix B). The committee also recommended that the SSRA include a much broader view of indirect economic effects. A summary of the committee's recommendations regarding the SSRA is provided in Box 1-3. DHS accepted the committee's recommendations and included the proposed changes in the SSRA work plan. On June 7, 2010, the committee chairman conducted a briefing on the preliminary letter report for staff members of the U.S. House and Senate Committees on Appropriations.

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[3]*Biosafety in Microbiological and Biomedical Laboratories (BMBL)* states that "exotic agents that pose a high individual risk of life-threatening disease [in humans] by infectious aerosols and for which no treatment is available are restricted to high containment laboratories that meet biosafety level 4 (BSL-4) standards" (CDC, 2009).

[4]*BMBL* states that BSL-3 is appropriate for "agents with a known potential for aerosol transmission, for agents that may cause serious and potentially lethal infections and that are indigenous or exotic in origin" (CDC, 2009). The BSL-3 agriculture (BSL-3Ag) designation is used for animal research facilities involving BSL-3 biological agents (such as foot-and-mouth disease) that present a risk of causing great economic harm if they infect the indigenous animal population (NRC, 2005).

Box 1-3
Summary of Recommendations from Preliminary Letter Report

The committee believes that the proposed work plan provided a reasonable framework but missed several fundamental issues related to the Manhattan, Kansas site and the unique requirements of a foreign animal and zoonotic disease facility.

1. The plan for the SSRA as outlined does not appropriately analyze potential pathways and will need to consider a better balance of other possible pathways of pathogen escape including, but not limited to, wastewater, fomites, and residual solid wastes.
2. The committee is concerned that the plan for the SSRA is limited to an examination of foot-and-mouth disease (FMD) and Rift Valley fever (RVF) viruses.
3. The SSRA will need to take into account the range of risk posed by working with the comprehensive suite of pathogens that are likely to be in the NBAF, including those at the BSL-4 level. FMD and RVF viruses do not represent the array of infectivity, vectors, hosts, environmental factors, and maximum credible risk scenarios that may result from emerging pathogens with unknown characteristics that require attention in the proposed high-containment facility.
4. The plan for the SSRA does not take into account the necessary laboratory training or management practices for establishing a competent, experienced, and credentialed workforce.
5. Mitigation strategies are not robustly or precisely addressed in the plan for the SSRA and will need to include other federal, state, county, and local officials to develop preparedness and response plans.
6. Determining the economic effects of an outbreak will require the SSRA to go beyond local market effects and include a national and international assessment that addresses additional commodities that would be affected by an outbreak.
7. Finally, to provide a more comprehensive and thorough SSRA, DHS and its contractors will need to consult additional subject matter experts, beyond those identified in the plan for the SSRA, to examine all the risk factors that need to be considered.

Final Report and Discussions with DHS

DHS and its contractors conducted the SSRA and delivered the report to the committee on June 30, 2010. The committee convened on July 13-14, 2010, in Washington, DC, to discuss the SSRA with DHS and its contractors (see Appendix C for meeting agendas). In attendance to answer questions related to the report were DHS officials and contractors that prepared the SSRA. During the open session of the meeting, the committee raised questions about the SSRA, and it submitted additional questions to DHS shortly thereafter. DHS delivered follow-up letters on July 28 and August 26, 2010; the latter follow-up letter provided a revised economic analysis, revised version of the SSRA's chapter 5 with edits noted, and a revised discussion of risk posed by high-velocity winds (both follow-up letters are included in an appendix to the SSRA).

Limitations of the Scope

As outlined in the Statement of Task and as mentioned in the preliminary letter report (see Appendix B), it was beyond the committee's purview to offer a judgment on the site location for the NBAF or to provide an interpretation of the SSRA for validating the site selection. The committee was restricted to assessing the adequacy and validity of the SSRA and was precluded from performing its own risk assessment. Accordingly, although the present NRC committee report discusses various aspects of the risk assessment, it contains no judgments about the wisdom of the selection of Manhattan, Kansas, as the site for the NBAF. This final report provides an evaluation of the SSRA and attempts to fulfill its two tasks: informing whether the risks were adequately and validly characterized for locating the NBAF in Manhattan, Kansas, so that Congress can make an informed judgment on the obligation of NBAF construction funds; and identifying ways for DHS to improve the biosafety and mitigation plans to ensure safe operations for the NBAF.

NEW CAPABILITIES OF AND RISKS POSED BY THE NATIONAL BIO- AND AGRO-DEFENSE FACILITY

Foot-and-Mouth Disease Virus Research on the Mainland

The plan to locate the NBAF in Manhattan, Kansas, reflects an important change in both policy and philosophy related to conducting foreign animal disease programs that use infectious (live) agents (especially FMDv) on the mainland of the United States. In accordance with 21 U.S.C. Section 113a, FMD research has not been permitted on the U.S. mainland since 1937, because FMD is a highly infectious disease of cloven-hoofed animals that has major economic consequences for international trade. Since 1954, the nation's foreign animal disease research and diagnostic programs have been conducted at the PIADC, which is on an island. Given the standard for infectious agent containment at that time, the original reasons for locating the facility on Plum Island were two-fold: first, the remote location would safeguard the country's livestock health (Plum Island is nearly 2 miles off Orient Point on the northeast end of Long Island, New York, and there are no livestock on Plum Island outside the laboratory); and second, the remote location would be relatively secure for conducting research on disease agents (the only allowed means of accessing the PIADC are by ferry or helicopter). Important advances in high-containment laboratory design, equipment, and work practices have occurred in the last 5 decades and have enabled DHS to determine that work on foreign animal diseases, including FMD, can be safely conducted on the mainland (DHS, 2009). FMDv work on the mainland would constitute a dramatic change in U.S. policy—a change that favors long-term world-class advances in research, diagnostics, and disease-control technologies while fueling concerns with some people and organizations. Canada and other countries already have such mainland capability.

The United States has been free of FMD since 1929 (USDA-APHIS, 2007). Because FMDv is the cause of major natural outbreaks in some parts of the world (Yang et al., 1999; Gibbens et al., 2001; Haydon et al., 2004; Anderson, 2008; Nishiura and Omori, 2010) and is housed in many international laboratories (OIE, 2009), there is a risk that it could be accidentally or intentionally introduced into the United States. NBAF will serve as the central U.S. asset in

supporting preparedness for and response to such an event. FMDv is exceptionally infectious in cattle and swine, and so poses an extraordinary risk to the U.S. agricultural livestock economy. That is especially the case for Manhattan, Kansas, which lies at the heart of the beef cattle industry and close to the heart of the swine industry. The impact of an FMDv release, regardless of whether it be from the NBAF or introduced into the U.S. from another source, would potentially be very high. Therefore, it will be important to use every possible means to prevent an escape and to mitigate the consequences of an escape.

High-Containment Work with Large Animals

The NBAF is expected to support substantial research and training activities using large animals that are infected with foreign animal disease agents and zoonotic pathogens of interest. It would present a new opportunity for scientists and disease control officials in the United States to study FMD and zoonotic diseases in large animals, new capabilities that would carry site-specific risks. Many laboratories around the world work on FMD in large animals with various levels of containment (OIE, 2009).

The NBAF would be the world's third facility to have BSL-4 laboratories that can work with large animals; the other two are in Geelong, Australia, and Winnipeg, Canada.[5] Research and training activities involving dangerous zoonotic pathogens in large animals will be new in the United States, and these activities are of great national economic, health, and security importance. However, the new capability for large animal work in BSL-4 rooms will pose unique risks that will need to be anticipated and prevented by appropriate facility design, modern biocontainment equipment and practices, and exceptional staff expertise and reliability. Only two zoonotic agents (Nipah virus and Hendra virus) have been considered in the SSRA for BSL-4 research with large animals, but it is clear that similar agents (including new agents and "unknowns") will need to be considered for future programmatic development at the NBAF.

Larger Experimental Animal Facilities

NBAF design plans indicate that it will have more than twice as many gross square feet as the PIADC and will include more BSL-2, BSL-3, and BSL-3Ag areas. Table 2-1 of the SSRA states that the PIADC has 31,868 ft^2 of BSL-3Ag space, compared with the planned 42,820 ft^2 of BSL-3Ag space in the NBAF. It is important to note, however, that the PIADC space does not meet the standard for a BSL-3Ag facility, because the BSL-3Ag designation set out in the *Biosafety in Microbiological and Biomedical Laboratories* reference manual (CDC, 2009) was developed after the PIADC was built and the PIADC has only a single HEPA (high-efficiency particulate air) exhaust system. Work on zoonotic pathogens requiring BSL-4 biocontainment has not been conducted in the PIADC. The NBAF will include not only large animal research in BSL-4 conditions, but will also include a Good Manufacturing Practice (GMP) laboratory with BSL-3 capability for master seed production for vaccine development (page 25 of the SSRA).

[5]The Australian Animal Health Laboratory (in Geelong) and the National Centre for Foreign Animal Disease (in Winnipeg) have set the standard for biocontainment of research and training activities involving dangerous zoonotic pathogens in large animals. That was done in concordance with long experience in BSL-4 laboratory work in several human disease laboratories, especially those at the U.S. Centers for Disease Control and Prevention (in Atlanta, Georgia) and the U.S. Army Medical Research Institute of Infectious Diseases (in Fort Detrick, Maryland).

PROPOSED SITE IN MANHATTAN, KANSAS

Proximity and Population

Manhattan is in Riley County and is approximately 120 miles west of Kansas City. The Manhattan community occupies about 18 mi^2 and has a population of about 50,000 (City of Manhattan, 2010). Kansas State University (KSU) is the largest employer and educator in Manhattan, with more than 23,000 students (KSU, 2010). The proposed site of the NBAF will be on the KSU campus immediately adjacent to the recently constructed Biosecurity Research Institute (BRI) and a short distance from the College of Veterinary Medicine's research laboratories and teaching hospital. The BRI has state-of-the-art BSL-3, BSL-3 Enhanced (BSL-3E), and BSL-3Ag research space. Major livestock operations and livestock transportation hubs are also nearby.

Natural Hazards

Kansas is in an area known as "Tornado Alley", a region with a disproportionately high frequency of tornadoes (NOAA, 2008). The last major tornado to touch down in Manhattan was an EF4 tornado that occurred on June 11, 2008, and caused an estimated $20 million in damages at KSU and destroyed portions of the Wind Erosion Laboratory (KAKE, 2008).

Kansas is not particularly prone to earthquakes, but some parts of the state are more earthquake-prone than others. A series of faults called the Humboldt Fault Zone runs through Riley County directly east of Manhattan (KGS, 1996, 2000).

Manhattan was built on a floodplain just east of where the Kansas River and the Big Blue River intersect. The Big Blue River discharges its waters into Tuttle Creek Lake, the second-largest lake in Kansas, which is about 5 miles north of Manhattan (USACE, 2004). The Army Corps of Engineers is conducting a seismic retrofit of the Tuttle Creek Dam (USACE, 2004). With heavy precipitation, the area is prone to floods and flash floods.

ORGANIZATION OF THE REPORT

The remainder of this report presents the findings and conclusions of the committee's evaluation. Chapter 2 examines site-specific risk and mitigation factors that should be considered for constructing and operating the NBAF in Manhattan, Kansas. Chapter 3 evaluates the methods used by DHS in the SSRA. Chapter 4 assesses the design plans and the plans for personnel preparedness, including the engineering and training needs to reduce the risk of a pathogen release from the NBAF and the effects if a release occurs. Chapter 5 presents the committee's overall assessment and findings about the adequacy and validity of the SSRA, and concluding remarks for the Congress and DHS in moving forward.

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2

Consideration of Site-Specific Risk and Mitigation Factors

A seminal risk assessment report *Risk Assessment in the Federal Government: Managing the Process* by the National Research Council (NRC, 1983) and a recent publication on *Quantitative Microbial Risk Assessment* (Haas et al., 1999) define risk assessment as "the qualitative or quantitative characterization and estimation of potential adverse health effects associated with exposure of individuals or populations to hazards (materials, situations, or physical, chemical, or microbial agents)." Risk assessment can be used as a tool to estimate the probability of an adverse event in a specified period. Risk management—which takes into account risk assessment and engineering, economic, legal, and political issues—is process of controlling risks, weighing alternatives, and selecting appropriate actions (NRC, 1983; Haas et al., 1999).

The Department of Homeland Security's (DHS's) site-specific risk assessment (SSRA) identified the following objectives for its report:

- "To inform the requisite design and engineering controls for the National Bio- and Agro-Defense Facility (NBAF).
- "To inform emergency response plans with city, regional, and state officials in the event of an accidental release of a pathogen.
- "To assist in the development of the operational protocols needed to safely and securely operate the facility.
- "To include an integrated set of analyses using plume modeling and epidemiological impact modeling."

The NRC report *Review of the Department of Homeland Security's Approach to Risk Analysis* recently evaluated the quality of the current DHS approach to estimating risk and applying those estimates in its many management, planning, and resource-allocation activities (NRC, 2010a). This report's evaluation of the SSRA is consistent with the findings, conclusions, and recommendations of that report.

SITE-SPECIFIC CHARACTERISTICS THAT AFFECT RISK

Factors Identified by the Department of Homeland Security

High-Risk Tornado Area

On average, 1,000 tornado events (ranging from 700-1,400) occur annually in the contiguous United States (Lott et al., 2000). Cold dry fronts coming over the Rocky Mountains in the spring travel south or east and then collide with moist air coming north from the Gulf of Mexico and cause severe thunderstorms (NOAA, 2010). The thunderstorms can develop into tornadic storms. A vast majority of U.S. tornadoes occur in the region of the Midwest that extends from northwest Texas to the Great Lakes in an area called Tornado Alley, which includes Manhattan, Kansas.

Vicinity as a Hub for Transportation of Cattle and Other Livestock

Key site-specific characteristics with respect to conducting research on foot-and-mouth disease (FMD) are the large number of susceptible animals in the immediate vicinity and the percentage of the U.S. herd in the region. Those issues are addressed by examining the animal population within a radius of 200 miles around Manhattan, Kansas. The area in question is primarily a beef cattle region that includes some dairy cattle and swine operations (USDA-NASS, 2009). A 200-mile radius includes most of Kansas, large parts of Nebraska and Missouri, western Iowa, and northern Oklahoma. Roughly 9.5% of the U.S. cattle inventory is in the area, and it includes substantial regions of swine production and several meat packing plants. In 2009, the total U.S. inventory for cattle and swine were 94.5 million head and 66.7 million head, respectively (USDA-NASS, 2009).

The SSRA recognizes that the area studied is "a hub of animal movement for the entire United States" and that "in reality, as infected animals are moved throughout the country, pockets of infection would be expected to occur great distances from the initial focus of infection" (page 176). If FMDv escapes from the NBAF, it is likely to cause a widespread and economically devastating outbreak of FMD because of the facility's proximity to a hub of animal production and transportation. It could cause major damage to the credibility of all federal agencies involved,[1] especially if rigorous and robust mitigation strategies have not been put in place. Such an event would probably have major consequences for future operation of the facility and the ability to work with FMDv on the mainland. Given that FMD is a highly contagious disease and that the chance of FMDv escape is not zero, it is essential that rigorous and robust regional and national mitigation strategies that address an extensive outbreak of FMD be put into place before the NBAF opens.

Factors Not Identified by the Department of Homeland Security

The Plum Island, New York, and Manhattan, Kansas, locations differ in proximity to human and animal populations. The Plum Island Animal Disease Center (PIADC) is on an uninhabited island, whereas the NBAF will be in a suburban-rural area that has a large human

[1]Credibility could also be jeopardized in the event of escape of a zoonotic pathogen if the infected workers lacked access to top-quality infectious disease expertise and facilities.

population and that is very close to susceptible animals. Those characteristics introduce site-specific risks that are important to consider for the NBAF but were not included in the SSRA.

Proximity of Metropolitan Area

The NBAF site in Manhattan, Kansas, is in a corner of the Kansas State University (KSU) campus directly adjacent to student housing, campus recreational facilities, and the university football stadium, which has a capacity of 52,200. Figure 2-1 shows the proximity of the planned facility to the local population at KSU. The large population that gathers for football games and other events is potentially susceptible to infections with a zoonotic agent; additionally, the presence of large numbers of vehicles during public events increases the odds that some will transport a released pathogen outside of the area, increasing the potential for spread and complicating mitigation. Although many high-containment laboratories are located in highly-populated areas, the SSRA failed to adequately account for such populations and the large animal aspects of the NBAF's work in its risk analysis.

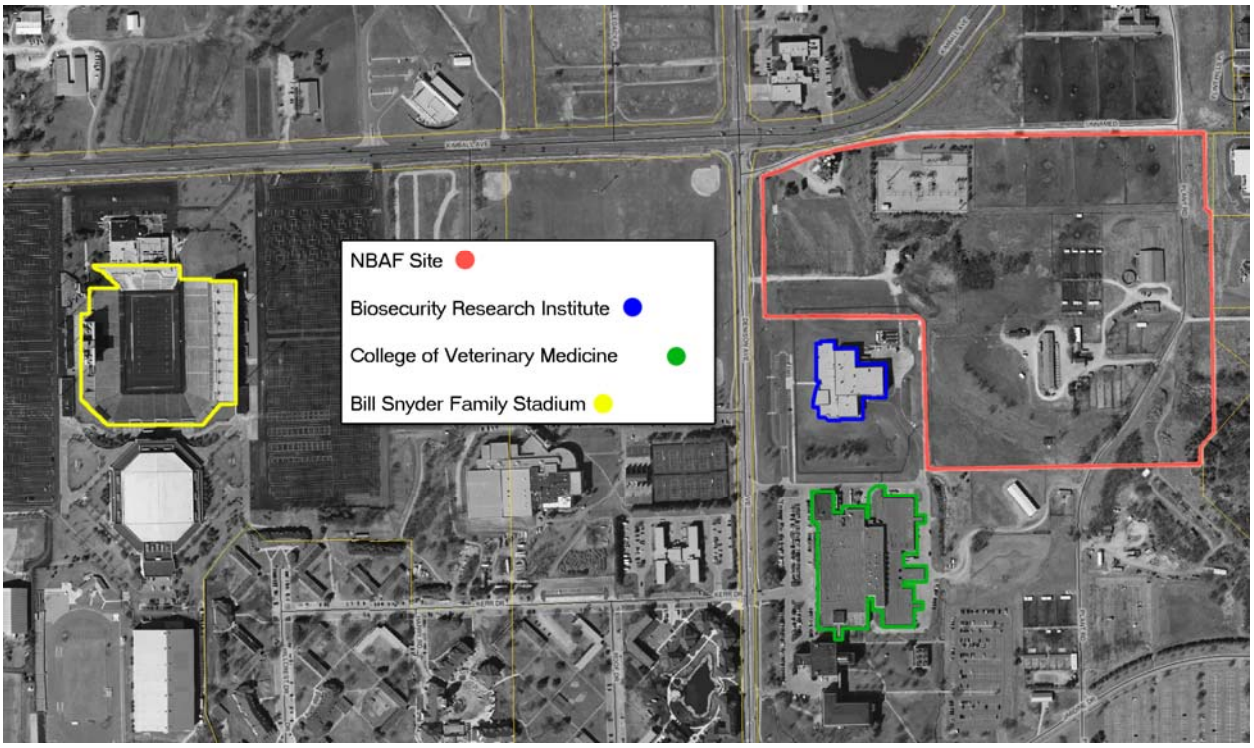

Figure 2-1 Map of the planned NBAF and the surrounding Manhattan, Kansas, vicinity. Kansas State University occupies most of the area shown in the map. The planned site of the NBAF is outlined in red. SOURCE: Riley County, October 2010. Map used with permission.

Proximity of Other Animal Facilities

The NBAF will be adjacent to the KSU Biosecurity Research Institute (BRI) and the KSU College of Veterinary Medicine. The purpose of the proximity is to facilitate interaction of

scientists in the NBAF with scientists in those two facilities, other KSU scientists, and those in the recently established DHS Center of Excellence for Emerging and Zoonotic Animal Diseases.

Locating the NBAF on the KSU campus would facilitate opportunities for training in foreign animal and zoonotic diseases. It is expected that the NBAF will continue the PIADC responsibility of providing foreign animal disease training to qualify veterinarians as foreign animal disease diagnosticians. The NBAF will also provide opportunities for training KSU graduate students and postdoctoral research associates. However, access to high-containment laboratories and animal facilities requires extensive training and certification, and this will limit the opportunities for those in training positions. Proper training, education, and monitoring of skills would reduce the risk of human error causing a release from the NBAF. Yet increasing the number of scientists, students, and postdoctoral scholars who have access to high-containment facilities would in all likelihood increase the risk of accidental spread of infectious agents via fomites, the primary identified risk in the SSRA.

One overlooked characteristic that would contribute to risk is the NBAF's proximity to KSU's College of Veterinary Medicine. Many susceptible animals at the college would be adjacent to the NBAF. Some of the animals may be housed on the campus, and others may travel to the campus for diagnosis and treatment and return home with their owners. If an agent were released from the NBAF, those animals could readily become infected and serve as a conduit for amplification and transport.

The National Centres for Animal Disease in Winnipeg, Canada, and the Australian Animal Health Laboratory in Geelong, Australia, have comparable biosafety level 3 agriculture (BSL-3Ag) and BSL-4 animal housing capabilities but on a smaller scale compared to the proposed NBAF. With regard to the risks associated with FMD research, there are major differences between these facilities and the proposed NBAF. The laboratory in Winnipeg conducts research on FMD, but the laboratory in Geelong is not allowed to conduct research on FMD. The Winnipeg laboratory has 14 BSL-3Ag rooms for housing FMD-infected animals. Thirteen of the rooms can each hold two head of cattle, and one room can hold four head of cattle. However, the Winnipeg laboratory typically does not have more than 8 animals infected with FMD at any one time. The laboratory also has one BSL-4 animal room which can hold two cattle. The nearest FMD-susceptible animals are in a zoo approximately 6-8 km away from the Winnipeg facility, and the nearest susceptible agricultural species are estimated to be 8-10 km from the Winnipeg facility[2] (Soren Alexandersen, National Centres for Animal Disease, personal communication, September 22, 2010).

SITE-SPECIFIC FACTORS THAT AFFECT MITIGATION PLANS

Clinical Capability for Handling BSL-4 Infections

The NBAF will handle zoonotic pathogens that cause disease in humans, including BSL-4 agents that do not have available treatment and can cause severe illness and death in humans. Clinical facilities and physician expertise will be important for responding to occupational

[2]The 8-10 km distance to the nearest susceptible agricultural species is significant because a radius of at least 10 km is the minimum distance that would be established for a control area around an FMD-infected premises in Canada (CFIA, 2008). A control zone with a radius of at least 10 km (6.2 miles) would also be established around each infected premises in the United States (Jon Zack, USDA-APHIS-VS, personal communication, January 26, 2010).

exposures (such as those leading to laboratory-acquired infections) and to releases outside the facility (such as those leading to community-acquired infections). That will require the presence of a sophisticated occupational medicine program to assess and manage potential exposures as varied as needlesticks and fomite and aerosol exposures. This may include hospitalization, isolation, and critical care of infected people and quarantine of contacts.

The SSRA provides a detailed analysis of the capabilities of the sole medical center that is close to the NBAF. Mercy Regional Health Center (MRHC), the major medical provider in the area, has a 150-bed hospital (normal census, 75-100 inpatients) that has nine isolation rooms (with negative pressure) in various locations around the facility, and it operates outpatient and related services in the municipality. The hospital medical staff includes a single infectious disease physician. There is also an Occupational Health Services group that provides services to KSU and BRI, and offers services such as respirator-fit testing and baseline serology assays. MRHC does not have the appropriate level of clinical isolation facilities, diagnostic laboratory capability, or world-class infectious disease clinicians experienced in diagnosing and treating for exposure to BSL-4 pathogens. It does not meet the standards of performance found at BSL-4 research facilities at the Centers for Disease Control and Prevention, USAMRIID, and the University of Texas Medical Branch (see NRC, 2010b for similar issues regarding laboratory-acquired infections in USAMRIID and the community's impact in developing response measures).

Regional Surveillance and Response Capability

Once the risk is estimated, prevention and mitigation strategies and preparedness and response plans will need to be developed as part of an overall risk management program. Rapid detection and response are important for preventing or minimizing spread in the event of a release of an infectious agent. The local and regional emergency response community will bear major responsibility in the event of an accidental or intentional pathogen release. Thus, the emergency management and response, medical, diagnostic, and surveillance capabilities of the NBAF and the surrounding community will serve as critical factors in response plans.

Human Health

On the basis of conversations with DHS and a meeting with local first responders and emergency management officials, the SSRA concludes that the area's emergency response capabilities are strong in a number of ways, such as a long history of cooperation, collaboration, and communication and a well-built emergency management organizational structure throughout the state of Kansas. The risk assessment team was in contact with representatives of MRHC, and the report contains a list of known and expected gaps in MRHC's readiness to deal with medical and other emergency responses for events at the NBAF. Furthermore, the risk assessment identified a gap in communication with health and medical providers, especially physicians. A possible way to improve communications is to use and expand the existing statewide communications network (the Health Alert Network) to send messages to key healthcare providers.

The SSRA states that the Manhattan, Kansas, area does not have adequate resources or capabilities to undertake all the prevention, mitigation, preparedness, response, and recovery activities necessary to develop and implement the emergency and contingency plans needed for

the NBAF. Apart from the information on MRHC and communication with health providers, the SSRA does not state what the specific gaps are, where the deficiencies occur, what capabilities are missing, or what plans have been developed to fix the insufficiencies. In other words, the SSRA lacks detailed analysis of the risks related to the emergency management and response capacities in the area. For example, other hospitals and medical providers within 20 miles of the proposed NBAF location were not evaluated as part of the risk assessment. The other health centers could be critically important in the event of an external release or a case of laboratory-acquired infection, but these rural and small community hospitals would not be able to handle the kind of outbreak that would involve a BSL-4 pathogen. A comprehensive analysis of regional health and medical assets is not included in the SSRA. The SSRA does not discuss the capabilities of local, regional, and state public health agencies, nor does it discuss surveillance and laboratory diagnostic systems.

Animal Health

The SSRA acknowledges the need to provide increased training and funding to the local and regional emergency response communities so that they can meet their increased obligations for detection, prevention, response, and recovery in the event of a foreign animal or zoonotic disease outbreak due to the presence of the NBAF in Manhattan, Kansas. The rapid response to a foreign animal or zoonotic disease outbreak will provide the greatest challenge to local and regional responders. Of particular concern is that there is no active national surveillance system for FMD detection. Passive surveillance is based on a traditional system in which practicing veterinarians report suspected “vesicular diseases”, and this would not be applicable to the zoonotic pathogens that would be in the NBAF. To fulfill the SSRA’s recommendation of enhancing local diagnostic capability to support regional surveillance and traceback capability, it will be essential to provide funding and validated tests to enable the National Animal Health Laboratory Network (NAHLN) at a minimum to conduct routine active surveillance for the agents under investigation in the NBAF. For an active FMD surveillance system to become fully operational, the NAHLN will need to expand its repertoire of testing and will need diagnostic surge capacity for those agents in the event of an outbreak. The KSU College of Veterinary Medicine Diagnostic Laboratory is a member of the NAHLN.

The SSRA recognizes that the Manhattan region serves as a hub of animal movement and could potentially allow infected animals to move great distances from an initial focus of infection, which would increase the likelihood of a widespread outbreak if FMDv escaped from the NBAF. In a widespread outbreak, USDA may implement an emergency vaccination policy for the outbreak areas as one of its response strategies. If such an approach is taken, then adequate supplies of vaccines, associated equipment, and trained vaccination teams would need to be available to respond to such an outbreak (as mandated for the National Veterinary Stockpile under Homeland Security Presidential Directive 9), and there will need to be a well-developed policy agreed to by all 50 states as to who would have priority for vaccine distribution.

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3

Evaluation of Methods

MAJOR MODELING ASSUMPTIONS AND ERRORS

Risk of Release

Assumed Low Frequency of Aerosol Release

Considering the various sources of spillage and the resulting aerosolization, the site-specific risk assessment (SSRA) made a key assumption about the frequency of aerosol release of foot-and-mouth disease virus (FMDv) that may result in an underestimation of actual risk. The estimated rate of 2.6 laboratory-scale spills per year is low, but no confidence intervals were given for the estimate, which would have allowed some assessment of a maximum-credible risk scenario.

The estimated spill rate is low for several reasons:

(1) In some instances, a person responsible for the spill either would not report it or would be unaware of it.

(2) The spill rate does not include the likelihood of spills from sample shipments or damage occurring during shipment. The National Bio- and Agro-Defense Facility (NBAF) may insist on the use of special shipping containers, but experience in other laboratories shows that not everyone will use them. Shipping containers will enter the NBAF from foreign countries where primary sample containers and shipping boxes, although required, may not meet U.S. regulations. The likelihood of spills caused by damage after a conveyance accident was not addressed in the SSRA (for example, a spill may not be immediately apparent on inspection of a container that is transported to the laboratory by a courier).

(3) Of greatest concern is the omission of anticipated virus spillage that would occur routinely as part of regular cleaning of large animal rooms. The NBAF will be equipped for biosafety level 3 agriculture (BSL-3Ag) and BSL-4 research with large animals. Rooms housing infected large animals that shed large amounts of FMDv (or other foreign animal or zoonotic pathogens) are typically washed down with water at least once a day, depending on the accumulation of feces, urine, and feed . The cleaning process will deliver kinetic energy (both through manual labor and through

high-velocity water) that will impact indoor air mixing regimes and will generate both aerosol and fomite loads, which were not appropriately considered in the SSRA.

Wash-down is likely to generate fine aerosol from shear, bursting bubble film, and jet droplets. The latter two mechanisms are known to generate an aerosol that contains a higher content of virions or bacteria per unit volume than what is found in the bulk water phase (Baylor et al., 1977; Hejkal et al., 1980; Blanchard and Syzdek, 1982). The wash-down process would aerosolize virus deposited in the room from animal secretions and excretions, and would result in removal of massive amounts of virus through the air filtration system. Even with the use of disinfectants,[1] the committee feels that those sources offer more frequent (daily) opportunities and possibly higher viral loading than the laboratory-scale spills that were evaluated in the SSRA. If only one room were used for FMD experiments, it would be the equivalent of experiencing 365 necessary and anticipated spills per year. Such a spill rate would raise the risk estimates by a factor of more than 140 from what is given in the SSRA (365/2.6 = 140).

An important factor that was neglected in the SSRA is the distinction between real and simulated conditions for viral disinfection and natural viral decay. The hosing of waste materials (such as secretions and excretions) would create a protective bioburden matrix for virus particles, and their aerosolization would lead to a severe underestimation of the amount and duration of potentially infectious material generated. The SSRA also did not address the effects of large amounts of aerosolized material (such as dust, dander, and other particles [such as fur, feed, vomit, cud, mucus, and hoof detritus]) on high-efficiency particle air (HEPA) filters in animal rooms and how it would affect filter performance over time.

Laboratory-Release Risk Estimates Not Based on Real World Experiences

The SSRA did not adequately consider case histories in arriving at risk estimates of laboratory leaks, and information from the documented cases of FMD releases were not fully taken into account. Although the NBAF will be engineered and constructed to a new level of safety, an examination of past FMD incidents from laboratory releases needed to have been considered in the SSRA. Between 1960 and 2007, there were 15 known escapes of FMDv from laboratories worldwide, with 13 occurring in Europe, 1 in Russia, and 1 in the United States (Anderson, 2008; GAO, 2008). Lessons learned from the escapes of FMDv from the Plum Island Animal Disease Center (PIADC) in 1978 (GAO, 2008) and Institute for Animal Health Pirbright Laboratory in the UK in 2007 (Anderson, 2008) appear not to have been applied in deriving reasonable expectations for risks of virus escape. When DHS was asked about this at the public session of the committee's meeting, a somewhat confusing answer was provided: that the escape from Plum Island (Margasak, 2008) was irrelevant because livestock were being housed on the island, and this will not be the case for the NBAF, which will be in Manhattan, Kansas. The facts remain that an FMDv escape did take place and that there are many cattle near the proposed site

[1]The protocol for the use of disinfectants at the NBAF has not been established nor was it discussed in the SSRA. Disinfectants would likely be used in the final cleaning of a vacated room, but routine use during an experiment would affect indoor air quality (and could impose human and animal health risks) and affect solid and liquid wastewater treatment (and could affect equipment performance). The use of disinfectants would still aerosolize particles and increase the risk of fomites. The complicated mix of organic solids and liquids present in animal rooms will serve as chemical and physical barriers to the intended microbial targets, and will thus reduce the predictability and efficacy of disinfection. This deserves careful consideration and a dedicated standard operating procedure to determine the appropriate cleaning and disinfection procedures and the dosing and delivery of disinfectants.

in Manhattan. In addition, the escape of FMDv from the Institute of Animal Health Pirbright Laboratory in 2007 has been reported to have occurred through a series of events that would seem highly improbable. The committee recognizes that the risk is not zero, and that unexpected events can result in an inadvertent release of FMDv.

The SSRA states that the estimated frequency of failure of the liquid effluent decontamination system is once every 2.1 million years. However, such a failure was the cause of the release of FMDv from Pirbright in 2007 (UK-HSE, 2007); and in June 1999, just before the National Centre for Foreign Animal Disease in Winnipeg, Canada, became operational with infectious agents on board, a batch of untreated wastewater was accidentally released into Winnipeg's sewage system (Löfstedt, 2002). Both incidents are well known and will raise questions about the SSRA's estimated frequency of once every 2.1 million years.

There have been many documented leaks of dangerous viruses from laboratories, including a leak of the Sabiá virus from a laboratory in Brazil (Lemonick and Park, 1994) and a leak of Venezuelan equine encephalitis virus from a laboratory in Colombia, which was cited as the likely cause of a human epidemic in 1995 (Brault et al., 2001). There have been leaks of FMDv from the Plum Island (GAO, 2008) and Pirbright laboratories, most notably the recent outbreak at Pirbright in 2007 (Derbyshire, 2007), which apparently was not considered in the SSRA. The committee believes that an assessment based on a plethora of information on case histories of escape of agents from laboratories would likely have provided a more realistic assessment of the case scenarios, likely frequencies, and confidence intervals of laboratory escapes projected for the NBAF.

Risk Uncertainties and Variation of Risk over Time Not Considered

The SSRA does not discuss or quantify uncertainties in the risk estimates. The *Review of the Department of Homeland Security's Approach to Risk Analysis* noted that "there is little understanding of the uncertainties in DHS risk models… and in addition there is a tendency toward false precision" (NRC, 2010), which was also the case with the SSRA. The risk estimates included in the SSRA are presented as single point estimate numbers to two decimal places, which implies a level of precision in the risk estimates that is likely unrealistic. While sensitivity analyses of several case model components were undertaken, the SSRA does not provide a quantitative assessment of the uncertainty surrounding the case event risk estimates (for example, in the form of confidence intervals) nor is there a qualitative discussion of the sources and magnitude of the uncertainties associated with these scenario risk estimates.

Furthermore, the SSRA neglected to consider how risk would vary over time. The annual risk estimates presented in the SSRA assume constant annual risks over the 50-year life span of the NBAF. However, annual risks will not necessarily remain constant over time because operating practices, experimental design and equipment, and staffing—among many other aspects—could result in either improvements or degradations that accordingly decrease or increase risks. The SSRA does not address the variation of risk over time in either a quantitative or qualitative manner. The potential for degradation and the subsequent means to address such risk were not considered in the SSRA.

Aggregate and Cumulative Risk

The SSRA failed to provide an appropriately aggregated assessment of cumulative risk over the expected life span of the NBAF. Although previous NRC reports have highlighted the need for assessing overall risk (e.g., NRC, 1994, 2009), the SSRA did not provide a cumulative risk assessment[2] for multiple agents and stressors by all routes and pathways to determine the overall risk of operating the NBAF in Manhattan, Kansas. At a minimum, the SSRA needed to have provided aggregate[3] risk, which is an essential component of risk characterization (NRC, 1994). The need to include lifetime risk estimates is consistent with the mandate included in the Homeland Security Presidential Directive 9 to "develop a plan to provide safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases," and is also consistent with the recommendation included in the 2008 National Research Council report that the Department of Homeland Security (DHS) address the probabilities of a sequence of events that would lead to a pathogen release (NRC, 2008). When the committee prompted DHS to provide an estimate of overall risk based on the completed risk assessment, the agency responded by stating that "the NBAF operations in Manhattan, Kansas overall brings extremely low risk relative to the greater risk of the intentional or accidental introduction of FMDv by an external source" (Response to question 1, DHS follow-up letter, July 28, 2010). The committee finds that the comparison is misleading because the SSRA does not consider or quantify the risk of infection from an external source. DHS responded furthermore that it was beyond its congressional mandate to determine an overall estimate of risk, and that the scope of the SSRA was limited to determining release scenarios and integrating their economic impacts (Response to question 1, DHS follow-up letter, July 28, 2010). On the basis of the release scenarios that were each deemed as "low risk", DHS ranked the scenarios by "risk dollar". [4]

There are several issues related to DHS's attempt to present estimates of risk. It is inaccurate to conclude that risk is "low" without further definition that would make its meaning less subjective. Although DHS did calculate risk by case frequency as cases per year (see Table 6-3 of the SSRA), it chose to present "risk" on the basis of economic consequences for a series of independent scenarios (see Table 6-4 of the SSRA). As indicated in Chapter 2 of the present report, risk assessment metrics often include the probability of an event over a period of time, yet the SSRA focused on single-year risks. The committee believes that it is misleading to convey risk in dollar amounts. The SSRA should have presented the risks for each scenario over the expected 50-year life expectancy of the NBAF, the associated costs (taking into account interest and inflation), and the cumulative risk for the NBAF with its expected lifetime operations in Manhattan, Kansas.

The committee found that the SSRA fell short of considering the cumulative effect of all independent scenarios and estimating the overall (cumulative) risk of release that would result in

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[2]The 2009 National Research Council report *Science and Decisions: Advancing Risk Assessment* defines cumulative risk as "the combination of risks posed by aggregate exposure to multiple agents or stressors in which the aggregate exposure is by all routes and pathways and from all sources of each given agent or stressor."

[3]According to the 1994 NRC report *Science and Judgment in Risk Assessment:* "An essential component of risk characterization is the aggregation of different measures and characteristics of risk: the risk assessor must communicate measures and characteristics of predicted risk in ways that are useful in risk management."

[4]The committee notes that the term "risk dollars" may be useful as a way of ranking risks to identify which actions have the highest payoff to mitigate the impact, but the term can easily be misinterpreted as a measure of annual mitigation costs or total dollars at risk.

infection with pathogens that will be handled in the NBAF. The case frequencies presented in Tables 6-3 and 6-4 of the SSRA are the products of the probability of pathogen release and the probability of infection in each scenario per year. The resulting frequencies of infection caused by laboratory release are difficult to interpret because they present individual risks without an overall risk of an index case over a period of 50 years.[5] Given the expected 50-year operational life span of the NBAF, the question is what the likelihood of a release and a disease outbreak will be in that period. Overall risk for the events listed in Table 6-3 of the SSRA could have been estimated by aggregating the annual frequencies of the scenarios leading to each independent event for each agent.

The SSRA failed to provide an overall risk estimate for the accidental release of even a single agent such as FMDv. A lower-bound estimate of the cumulative risk of release that results in FMD infection over the NBAF's 50-year life expectancy can be obtained by using the sum of two of the SSRA's scenarios with the greatest risk of FMDv release from Tables 6-3 and 6-4 (FMDv fomite personal contamination and FMDv worker with no respiratory protection). Figure 3-1 illustrates the results of the overall risk calculation[6] for FMDv. Over the NBAF's 50-year life span, the probability of an FMD infection from a laboratory release approaches 70% (100% would be absolute certainty), which the committee does not consider to be low. Even if the risk scenarios were not aggregated and if the top scenario of FMDv fomite release were the only risk considered, the SSRA estimates still show a probability that is not low. With the SSRA showing an accidental FMDv fomite release[7] leading to an infection recurring every 77 years and costing a mean of $32 billion (Tables 6-3 and 6-4 of the June 2010 SSRA), such an event has a 48% probability of occurring over the expected 50-year life span of the NBAF, assuming that the SSRA estimates provided for the committee's evaluation are accurate. The committee notes that these numbers probably represent conservative estimates because the SSRA overlooked other factors that would elevate risk.

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[5]The case summary tables for FMDv worker with and without respiratory protection (pages 117 and 118 of the SSRA) do contain assessments of the event frequency for the projected 50 year operations of NBAF. These two FMDv events are for fomite carryout and are important findings of the SSRA. However, the SSRA does not aggregate independent events such as these two examples to give an overall estimate of the operational risk by all scenarios for the operational life span of the NBAF.

[6]For the two scenarios with the greatest risk of FMDv release provided in Tables 6-3 and 6-4 of the SSRA, the total probability of a release that results in an index case is 2.33% for any year. Figure 3-1 of the present report was generated by using a binomial distribution and assuming that pathogen release during any year is a Bernoulli trial with a probability of infection of 0.0233. A Poisson distribution based on an infection frequency of 0.0233 per year yielded similar results. Regardless of the distribution used to calculate the probability, the probability that at least one index case (infection) will occur in 50 years is about 70%; this is a lower-bound estimate and not the overall risk for all scenarios in the SSRA. This number assumes that risks are constant and it does not account for the variation of risk over time. As such, it is an approximation of the cumulative risk over 50 years of operation. Some risk factors will change over time: some likely will increase risk as the facility ages while others may lower risk due to improvements in technology and practice and planned mitigation strategies at the NBAF.

[7]The SSRA states on pages 329-330: "For FMDv, the vector-to-susceptible animal transmission rates varied widely and many approached 100%. Thus, it was decided to use $P_i = 1x10^0$ for the probability of infection given an accidental FMDv release through the fomite/vector/pathway. It was recognized that this probability is high, but it represented the probability of the pathway and was appropriate for the vector case."

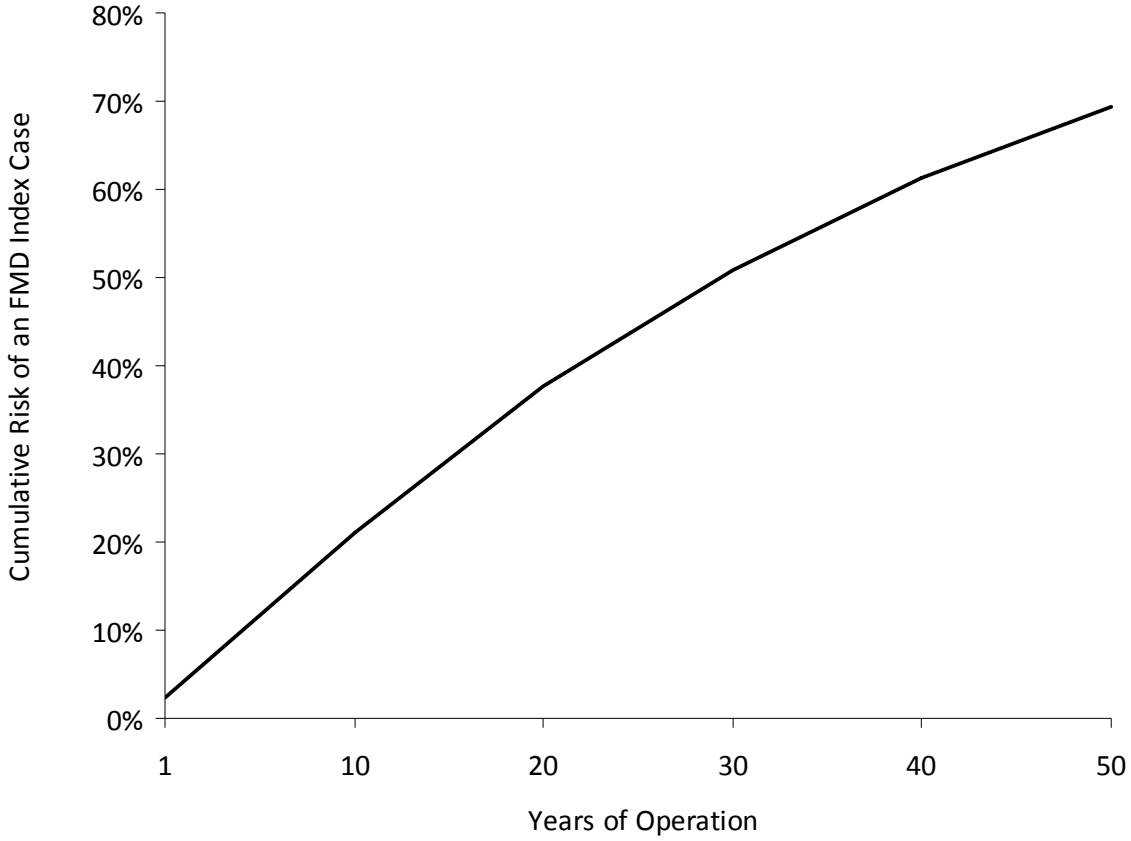

Figure 3-1 Risk of release that results in FMD infection over the life span of the NBAF. The probability was estimated by summing the risk from the two scenarios in the SSRA's Table 6-4 that had the highest risk (FMDv fomite personal contamination and FMDv worker with no respiratory protection).

MODELING CRITICAL TORNADO AND AIR DISPERSION SCENARIOS

Wind and Tornado

Model Used by the Site-Specific Risk Assessment

The SSRA analyzes the likelihood of tornadoes in Manhattan, Kansas, on the basis of tornado data on 1950-2009 archived at the Storm Prediction Center (SPC) of the National Oceanic and Atmospheric Administration, the only dataset available for assessing the risk of tornadic wind speed and associated effects. The SSRA shows tornado tracks from 1950-2009 covering a rectangular area of 29-43° latitude and 91-105° longitude; the NBAF is near a corner of the rectangle. In addition to the recorded tornadoes, the archived data are enhanced by potentially unrecorded tornadoes by using the method advanced by Ray et al. (2003). The enhancement is generally not performed to assess tornado risk although it provides a

conservative answer for tornado risk because it predicts additional tornadoes that are not part of the SPC dataset.

The SSRA's enhanced tornado data were analyzed statistically for frequency of tornado occurrence in an area surrounding the NBAF site. The analysis roughly predicted the occurrence of tornadoes of a particular F-scale intensity[8] in a fairly large box of 10 km square and yielded a mean return period of 77 years for tornadoes with F2 or greater intensity and a mean return period of 300 years for tornadoes with F3 or greater intensity (Table 5 in Appendix H of the SSRA). It did not predict wind speed versus time (or the mean recurrence interval) for the Manhattan, Kansas, point location. The analysis failed to include the area-intensity relationship and failed to assess the probability that a point would experience tornado wind intensity.

The SSRA states that design and construction will provide structural integrity and continued containment if the NBAF is in the direct path of a tornado of F2 intensity (or a wind speed range of 113-157 mph). The tornado scenario in the SSRA assesses the risk of a direct hit of the facility by a tornado of F3 or greater intensity, and it makes a poor assumption that the release would be minimal even if the facility were damaged and containment were lost. To justify that assumption, the SSRA is forced to make several subjective judgments so that it can consider a release or accident to be a rare event.

Alternative Model for Determining Wind Speed

A site-specific probabilistic tornado wind hazard model developed by the Lawrence Livermore National Laboratory (Boissonnade et al., 2000) has been used by the Department of Energy in developing design evaluation criteria for its facilities (DOE, 2002). The use of a tornado hazard model would provide a more accurate assessment that correlates tornadic wind speed with the annual probability of occurrence (or the mean return period) for Manhattan, Kansas. Its use would eliminate the need for subjective judgment on the low probability of overlap of tornadic wind speed and the NBAF site. In addition, a tornado hazard model could provide the specificity needed to determine specific wind speeds and a given time period rather than a range of wind speeds related to F-scale tornado categories.

In response to Question 43 from the committee (follow-up letter, August 26, 2010), DHS outlined preliminary plans for conducting a tornado wind hazard model for the final edition of the SSRA. However, the results of the planned tornado hazard model to be pursued by DHS were not available for the committee's review, thus it is not possible to comment on its efficacy.

In wind climatology, there is an inverse relationship between wind speed value and the probability of tornadic wind speed occurrence, and that relationship is shown as a continuous plot of wind speed v. probability of occurrence. If a rare wind speed event of 1×10^{-5} per year or less is chosen on which to base building designs, the facility envelope can be designed to provide greater containment protection to prepare for a rare high-wind event.

[8]As of February 2007, the National Weather Service replaced the F-scale with an EF-scale. The archived tornado data were recorded in terms of the F-scale. The development of the EF-scale includes correlation of wind speed on both F- and EF-scales, and this correlation is provided in the Enhanced Fujita scale report (McDonald and Mehta, 2008). If the tornado hazard model for the site is developed to yield wind speed on the F-scale, the wind speed for tornado risk and design can be translated to equivalent EF-scale wind speed. It should be noted that all tornadoes after February 2007 are categorized in terms of the EF-scale. Accommodation should be made in combining data before and after February 2007. The Nuclear Regulatory Commission has used the EF-scale in updating its requirements for nuclear power plants (Nuclear Regulatory Commission, 2007; Ramsdell and Rishel, 2007).

The facility envelope will need to be designed on the basis of the determined wind speed and not used merely for the facility's structural integrity; if the envelope of the facility is properly designed, there will be little chance of pathogen release to the atmosphere. The design-basis wind speed obtained from the tornado hazard model may or may not be higher than that of the F4 tornado that occurred in 2008 in the Manhattan, Kansas, vicinity.

Engineering best practices do not dictate that facilities be designed for the most severe event that may have occurred in the past or that has a chance of occurring in the future. Relying on information from a reliable tornado hazard model assessment and relying on the inherent resistance in building materials and the structural framework, the committee is confident that a facility can be built to withstand high-wind events and provide a safe environment in the rare event of an occurrence such as a high-intensity tornado.

Aerosol Formation and Dispersion

Estimating the risk of infection in animals through exposure to airborne virus particles consists of modeling the following processes:

1. Release of virus particles.
2. Transport, dispersion, and deposition of the released particles.
3. Survival of the virus particles.
4. Inhalation of air that contains ambient concentrations of virus particles that have undergone processes 2 and 3.
5. Infection associated with dose.

Virus particles released over a short period are modeled as a "puff" of material that increases in size as it travels from the source to a receptor. The concentration of virus particles in the puff depends on meteorological variables (such as wind speed and turbulence) that govern the transport, dispersion, and deposition of the released material. It also depends on ambient temperature and relative humidity, which determine the viability of the virus. The concentration in the air also depends on the size distribution of the virus and on the properties of the surface on which the virus is deposited.

For an aerosol that contains infectious virus particles, the infectious dose (ID) is the number of virus particles inhaled as the puff travels past an animal.[9] The ID determines the risk of infection caused by the virus. The dose is calculated by summing the virus particles in the air that is inhaled as a puff passes over the animal. The ID depends on the breathing rate of the animal and the concentration of the virus particles in the air. For a highly contagious disease, such as FMD, the risk of infection corresponds to the collective dose to all the animals exposed to the puff of virus particles. Thus, the dose calculation requires summing the doses to all the animals exposed to the puff of virus particles. If enough animals are exposed, infection may be likely even if the doses are very small.

[9]The SSRA uses the terminology "0.1 plaque forming unit (pfu)" to estimate the risk that escaped virus will cause infection in animals. The use of the term pfu is vague, unverifiable, and inconsistent with contemporary means for quantifying virus and estimating a minimal infectious dose. In the preliminary letter report, the committee recommended using a low infectious dose for determining the likelihood of infection. For the rest of its final letter report, the committee uses the more accurate terminology "0.1 virus particle".

Appropriateness of the Second-Order Closure Integrated Puff Model

In general, the SSRA follows accepted approaches to modeling the risk of airborne infection whereas the earlier environmental impact statement (EIS) did not. The EIS used a simple Gaussian dispersion model to estimate doses associated with a continuous source of virus particles at distance of 10 km. It did not go beyond suggesting that the dose at 10 km was less than the assumed minimum ID of 10 virus particles. The SSRA responds to the Government Accountability Office's valid criticism of the EIS by recognizing that the releases occur over a short period compared with the travel time from the source of material to the receptor.

The transport and dispersal of the resulting puff is modeled with the Second-Order Closure Integrated Puff (SCIPUFF) model (EPA, 2000; Sage Management, 2010). Although SCIPUFF is not the preferred model for regulatory applications, it is clearly a model with a solid scientific foundation and is one of the best models available. SCIPUFF is one of few models that incorporate realistic dispersion of instantaneous releases. It also incorporates the complex processes that govern transport of virus-containing aerosols, and this makes it a complex model with a large number of inputs, outputs, and options. That complexity can lead to errors in inputs that lead to errors in outputs. It is not clear from the SSRA that tests have been conducted to check for calculation errors.

The SCIPUFF model is used to simulate a number of hypothetical releases. The effect of those releases is measured in terms of the area over which the inhaled dose exceeds 0.1 virus particle. The minimum value of 0.1 virus particle is based on the argument that in a group of animals, a small number might be exposed to one virus particle that results in infection whereas the majority would not inhale any pathogens. The assumption is made to decouple the dispersion calculations from the epidemiological modeling. The SCIPUFF model calculations provide contours within which the dose exceeds 0.1 virus particle. Those contours are then superimposed on livestock distribution maps for the epidemiological modeling. If a farm or facility where livestock can be infected lies within a contour, all the animals in the premises are taken to be infected.

Criticism of the Method

The probability of infection is sensitive to the size of puffs released and to the number of releases during a period of time. Small laboratory spills that are estimated to occur 2.6 times per year are much less important sources of risk than the daily washing of animal pens, which has the potential to aerosolize much larger numbers of virus particles. Even with the use of disinfectants during cleaning of the animal pens, the daily cleaning of animal pens will probably result in releases that far exceed the 10^3 virus particles that are estimated to be released when a container is dropped even when a HEPA filter is functioning properly; the "material available for release" is likely to be much larger than the 10^{12} assumed in the SSRA, and the aerosolized fraction will be larger than the 10^{-4} value assumed for an accidental spill from a container. Because the probability of infection depends on both the amount of release and the frequency of release, a binomial model for infection indicates that even a small infection probability of 0.01 for an individual release translates into a 63% probability of infection when there are 100 releases, which corresponds roughly to the number of releases resulting from pen cleanings per year.

It is not clear from the SSRA that the arbitrary value of 0.1 virus particle represents a sharp cutoff that would exclude premises with a slightly smaller dose (such as 0.099 virus

particle) from the risk of infection. The assumption of a minimum dose could have been avoided by calculating the integrated dose over the group of animals exposed to a puff of virus particles. That approach would have required the dispersion calculations to explicitly account for livestock distribution in computing the integrated dose. The dose could then be related to the risk of infection at any specified location relative to the release location.

DHS has added information on exposure distances to supplement the exposure areas presented in Tables 3-31 and 3-32. These distances have the same problem as the impact areas: they are based on the arbitrary cutoff of 0.1 virus particle. Furthermore, they do not reflect uncertainties in meteorological variables, surface parameters, and emission strength. The exposure distance is directly proportional to the emission of viruses, which could be much higher than the 10^3 FMDv particles assumed for routine releases.

The largest doses are likely to occur when the boundary layer height is small, the wind speed is low, and the period over which the virus is viable is long, the dry-deposition velocity is low, and the relative humidity and temperature favor FMDv viability. That corresponds to stable, low-wind speed conditions in which meteorological models are notoriously unreliable (Luhar et al., 2009). Furthermore, several inputs cannot be specified objectively, such as the surface parameters (for example, roughness length). That suggests a need to conduct sensitivity studies to examine the effects of uncertainty in meteorological variables and values of model parameters on predicted doses.

The SSRA assumes that the variation in meteorological inputs captures most of the dose variation associated with uncertainty in model inputs. That assumption implies that the distribution of modeled doses will be close to that of observed doses—an assumption that needs to be justified by showing that variations in values of surface parameters have only a small effect on computed doses.

In response to how input uncertainty is accounted for in the models, DHS states that “due to the computation burden of fully exploring the entire parameter uncertainty space associated with these inputs, ‘reasonable worst case’ estimates were used” (Response to question 4, DHS follow-up letter, July 28, 2010). However, the SSRA does not provide information on the release and meteorological conditions that constitute a “reasonable worst case”, so thus the committee could not judge the validity of that approach for treating model uncertainty.

The results presented in the SSRA suggest that the horizontal scale of the effect of accidental releases of FMDv is in tens of kilometers. Under these circumstances, it might have been appropriate to assimilate the Manhattan Regional Airport meteorological data into the database constructed by Rife et al. (2010), which has a relatively coarse resolution of 40 km. The appendix to the SSRA states that the Rife et al. database was constructed to “recreate the observed characteristics of the Great Plains Nocturnal Low Level Jet”; however, there are no references to support the SSRA’s claim that the dataset was “specifically developed and subsequently validated to support boundary layer aerosol transport and dispersion modeling applications” (SSRA Appendix J: Aerosol Fate and Transport (Plume) Modeling).

The use of site-specific meteorology, such as that available from the airport, is likely to be important in developing emergency response plans for an accidental release of virus. Because the airport might be the only source of meteorological information during an actual emergency, it is important to run scenarios corresponding to airport data. If resources are available, the results will need to be evaluated with data from tracer studies at the NBAF location.

EPIDEMIOLOGICAL MODELING

The SSRA applied the North American Animal Disease Spread Model (NAADSM), a stochastic model used to obtain multiple simulations of the hypothetical spread of FMD in a primary modeling region that included neighboring states after the establishment of index cases resulting from various FMDv escape scenarios. The simulation runs generated probability distributions for the number of animals destroyed and durations of FMD epidemics in each scenario. Sensitivity analysis was conducted to determine how the probability distributions changed in response to various initial conditions, assumptions, and parameter values, including some related to mitigation.

Overall estimates of epidemic magnitude and duration were used as the bases of the SSRA's economic analyses. The epidemiological modeling component of the SSRA provides key inputs to the economic assessment, thus any concerns about that component will affect the economic analyses and conclusions of the SSRA.

The SSRA demonstrates substantial effort in modeling FMD spread, given the short period of time to conduct the assessment and the absence of critical data and well-documented assumptions for many parameter values. In particular, the SSRA team made a clear and constructive effort to collect data and estimate values for model parameters, including attempts to estimate locations of livestock herds throughout Kansas and nearby states.

Overall Concerns

The SSRA is unclear as to how the specific mitigation parameter values were determined, in part because of the inherent complexity of the NAADSM (Schoenbaum and Disney, 2003; Harvey et al., 2007) but also in part because of the SSRA's focus on a more general analysis. The ambiguity could theoretically be partially alleviated by the existing documentation and openness of the NAADSM. In practice, however, applying parameter values and interpreting the NAADSM results for the risk assessment will require personnel who have NAADSM expertise and familiarity with veterinary epidemiology.

In computational epidemiology, it is common to conduct sensitivity analyses of model outcomes in terms of model parameters. However, model parameters are usually phenomenological representations of subprocesses that the model makers have chosen not to include for reasons of insignificance, efficiency, uncertainty, or simplicity. In the case of this SSRA, realistic constraints on mitigation measures—such as supply, cost, and efficiency—have been lost because of particular modeling decisions. Without realistic constraints to provide context, outcomes from simulation of mitigation measures and associated sensitivity analyses cannot be turned into practical recommendations.

The quantitative epidemiological study in the SSRA provides a systematic and reasonable description of the distribution of outcomes in light of variations in mitigation rates. However, it does not connect the general mitigation rates to the logistics of specific mitigation practices in a site-specific manner. For instance, the SSRA uses a baseline culling rate of 120 herds/day (page 230) but does not consider the logistical demands that culling would place on personnel and equipment, nor does it allow an emergency response manager to gauge the reasonableness and relevance of the baseline scenario. The report also observes that an outbreak's risk can be "nearly completely mitigated" by active surveillance (page 225), but it does not discuss what implementation measures this would require. Those broad concerns about the overall validity of

the current quantitative epidemiological analysis of mitigation also apply to some of the results. Figure 4-20 of the SSRA, for instance, shows a bimodal distribution of epidemic outcomes. The bimodal effect may be due to random differences in initial condition, as suggested in Figure 4-14 of the SSRA, but bimodality over the given range of 3-6 million animals is surprising. It is well known that the probability an index infection leads to a widespread epidemic will depend on an initial chain of transmission events that is difficult to predict, and will depend strongly on location and the local environment. However, when an index case initiates an epidemic, modest transmission between locations is usually sufficient for final epidemic sizes to be independent of index-case location, particularly with respect to FMD. That suggests that the cumulative distribution in Figure 4-20 of the SSRA may be an artifact of specific model assumptions placed on contact patterns and mitigation. Evidence is presented (page 233, for instance) that epidemics are primarily limited by density and geographic characteristics rather than by mitigation measures, but this requires further elaboration by DHS inasmuch as many disease outbreaks are contained by mitigation strategies.

Specific Concerns about Model Adequacy

Exclusion of Species or Groups

The committee is concerned about the exclusion of specific species or management-type groups, such as “backyard” operations, sheep herds, and feral swine (the committee recommended inclusion of the latter in its preliminary letter report, see Appendix B). Backyard operations involve relatively small numbers of animals and often sell off stock at auction yards and purchase animals from other herds. They typically do not use veterinarians, and their activities would fall outside the scope of a passive surveillance system. Whereas few data on backyard operations would be available, such operations would contribute substantially to the spread of FMD from a primary source, and the spread rate would be much higher than that associated with typical commercial livestock operations (Bates et al., 2003). Similarly, the time until detection in such settings would be longer than for commercial operations.

Sheep make up only 1% of Kansas herds, but other states have a much higher percentage of sheep. Sheep and goats serve as maintenance hosts for FMD infection because they typically show few clinical signs of infection and can shed virus for extended periods. In the UK epidemic of 2001, sheep were a primary reservoir for infection and contributed substantially to the spread of the disease (Haydon et al., 2004). Feral swine would be important to consider in that they would probably become infected and be outside the passive surveillance system. In some of the states studied, feral swine are considered as posing a high risk for FMD spread. Thus, the exclusion of sheep and feral swine from the model leads to underestimation of the magnitude and duration of an FMD epidemic.

Limited Number of States Considered

The committee advised in its preliminary letter report that the SSRA consider the entire nation, or more specifically the 48 contiguous states, when modeling the epidemiological and economic impacts of FMD. However, the SSRA selects only seven “primary” states to consider in the model; the states were selected on the basis of their cattle and swine populations. A study limited to a few states is unlikely to reflect the impact of an FMD epidemic in the United States

as a whole, and assuming that the disease stays within the borders of seven states and within the borders of the United States, it is unlikely to reflect the complex geometric progression of the disease. The issue is not whether one should be concerned about states that have large or small livestock populations; rather the concern should be about how FMD is being transmitted within and among states and/or Canada and Mexico[10], and how livestock management and transportation practices and policies among all states, Canada, and Mexico would retard, sustain, or speed FMD spread throughout the United States. States that have small animal populations might actually have more sales barns, more garbage-feeding operations, and less stringent animal inspection policies than states that have large animal populations; these characteristics would increase the likelihood that FMD would be acquired by states that have fewer animals, would be disseminated within those states, and would spread to other states. Failure of the model to include the other 41 of the 48 states as well as incursions in and out of Canada and Mexico would clearly be manifested as unrealistically low estimates of the overall impact of FMD in the United States. Exclusion of states that are at high risk for acquisition or dissemination would probably further bias expectations toward an epidemic of low magnitude and short duration.

Lack of Long-Distance Transport Data and Method

The SSRA notes that a key weakness of the NADDSM is its inability to consider secondary FMD transmission between states or even between regions within a state. The SSRA notes that efforts at "model enhancement" (page 175) or development of "secondary models" (page 168) were undertaken to address that shortcoming, but it is unclear whether these are the same. The enhanced model is described imprecisely, and the committee could not determine the complete details of its implementation from the material supplied. In addition, the enhanced model inherits most of the limitations of the standard NAADSM, which may introduce substantial biases when applied on larger spatial scales than NAADSM was intended to handle. Thus, the ability of the overall modeling effort to reasonably and adequately estimate and account for interstate transmission of FMD remains an important question and casts doubt on results and conclusions drawn from the model.

Instead of developing a scenario-specific model, the SSRA addresses some of the contact-pattern issues across state boundaries by adjusting the NAADSM to include "sales barn" units, which facilitate "long-distance" dispersal. This adjustment is described in a general way that requires detailed understanding of the NAADSM design framework for implementation and replication. To determine the parameters for the long-distance dispersal mechanism, the model estimated cattle movements through sales barns in such a way that the sum of interstate movements among all sales barns equaled expectations for total interstate movement rates. Thus, sales barns were used as a surrogate for between-state transport livestock activities from all other possible sources, including large independent cattle operations; movements resulting from private sales appear not to have been considered. The primary justifications for assuming sales barn transport as a surrogate were concerns about model complexity and identifiability. While adding sales barns to the NAADSM is an improvement because it takes some interstate animal movement into account, sales barns are not the sole source of long-distance animal movement

[10]The SSRA did not fully consider modeling disease spread across state and country borders. Modeling disease spread with artificial boundaries (such as politically-designated state and country lines) creates a dilemma about how to deal with spread across country borders (into Canada and Mexico) and how such spread could be transmitted back across the border to impact spread in the primary area of interest (the United States).

rates (USDA-ERS, 2003), and therefore the SSRA underestimates the long-distance transport of animals and equipment and in doing so also underestimates the rate and extent of FMD spread.

Even if use of sales barns as surrogates for all interstate transport were sufficient for estimating total epidemic size, it introduces difficulties in assessing mitigation measures. There are differences in interests, regulation, and responsiveness between sales barns and large independent cattle operations that mitigation practices should consider. Specifically, the assumption leads to overestimation of the effectiveness of baseline mitigation measures, which therefore leads to an underestimation of the epidemic magnitude.

Highly Optimistic Detection Times

Both the time to develop clinical signs (lesions) and the time to detect (and report) clinical signs once they appear were considered in the model (pages 179 and 219 of the SSRA), but location-type-specific observation rates were not adequately documented. Some assumptions were made that probably resulted in an overoptimistic time to report a case of FMD, which would be manifested in limiting the simulated spread of disease and would bias results toward fewer cases and shorter duration.

Many of the data used to compile distributions of time to lesion appearance were obtained from experimental studies that examined the oral cavity and feet of animals for evidence of lesions (erosions and vesicles) once or twice a day after exposure to large doses of FMDv. Because a broad spectrum of immunological, inflammatory, and secondary infection events follow lesion development, the actual signs of frothing or lameness typically may not appear for some days after the first oral or foot lesions appear, depending on exposure dose, strain, and so on. For some species, such as sheep and goats, lesions may never appear or may be so subtle that they are missed entirely, as was observed in the UK epidemic (Haydon et al., 2004; McLaws et al., 2007), so exclusion of these species from consideration would result in a low estimate of FMD spread. Consequently, the time to appearance of "gross" clinical signs sufficiently apparent to be observed by a layperson would extend beyond when lesions first appear, perhaps by several days. Furthermore, it is overoptimistic to assume that the probability of detection and reporting would be 100% within 6 days (page 265) of when lesions begin to appear. On some premises, livestock may not be observed more than once a week. There is reason to believe that detection and reporting times could be months or more in some cases, as was observed in the Canadian FMD epidemic in 1952-1953 (Sellers and Daggupaty, 1990). Anecdotal statements of U.S. veterinarians who participated in the control program in the UK in 2001 indicated that very long delays may be expected between lesion development and reporting.

The assumption that "self-announcing" leaks from the NBAF (page 182) would result in even more rapid detection of cases around the laboratory is unrealistic given the process that would have to be involved in detection. It is unlikely that livestock owners would tolerate having their animals inspected (requiring lock up, oral inspections, swabbing, and so on) each day for weeks after a possible breach of containment in the NBAF. It is also unlikely that sufficient personnel would be available to conduct such investigations each time a breach were suspected.

Overestimated Diagnostic Capabilities and Sensitivity

Several important aspects of the clinical diagnostic sensitivity and of the laboratory diagnostic capability and sensitivity for FMDv were not considered in the modeling. In the case

of a suspected or actual release of FMDv from the NBAF, the laboratory will need to take special precautions and procedures that could adversely affect its ability to perform diagnostic testing. If the facility needed to shut down (for example, physical breach caused by a tornado or suspected pathogen leak from the laboratory), diagnostic support for necessary investigation and mitigation of a suspected escape may be compromised. When an FMDv release occurred in 2007 from the Institute of Animal Health Pirbright Laboratory in the UK, some FMD work at that facility was halted, including work on vaccines that could have been necessary had the FMD outbreak not been controlled (Anderson, 2008). The NBAF design plans include a pilot scale GMP manufacturing facility with BSL-3 capability (Figures 1-1 and 3-2 of the SSRA), which could produce very high concentrations of FMDv and other pathogens for vaccine production. As previously noted, there were 15 known escapes of FMDv from laboratories worldwide between 1960 and 2007 (Anderson, 2008; GAO, 2008), with most of those escapes occurring from vaccine manufacturing facilities that produce very large amounts of virus (Anderson, 2008). The SSRA does not provide contingency plans for auxiliary diagnostic support by other laboratories (such as state laboratories and the Winnipeg and Pirbright laboratories); such diagnostic contingency plans are critical for NBAF operations and should have been included in the SSRA.

The NAADSM uses a sensitivity value of 1.0 (1.0 being perfect accuracy) in identifying FMD-affected premises and assumes that the clinical diagnostic processes involved in contact tracing would be reliable and accurate. However, the 2001 UK epidemic demonstrated that sensitivity is not perfect and that it may be around 0.947 (McLaws et al., 2007). On the basis of that estimate, clinical monitoring and declaration could miss about 5.3% of infected herds. The existence of infected but undetected premises, referred to as occult infection premises (Jewell et al., 2009), is in part related to the exhaustion of resources needed to undertake trace contact investigations (Ferguson et al., 2001a,b; Keeling et al., 2001); the efficacy of contact tracing can be diminished considerably by resource constraints (Eames and Keeling, 2003; Kao, 2003; Kiss et al., 2005). As a consequence of the poor efficacy of contact tracing experienced early in the 2001 UK epidemic, a "contiguous cull" policy was implemented whereby animals in high-risk premises were destroyed, without diagnostic confirmation, in order to rapidly eliminate potentially infected premises (The Royal Society, 2002; Haydon et al., 2004). The failure of the SSRA to consider less than perfect diagnostic efficacy in the contact tracing is not a trivial omission in modeling the spread of FMD, and would probably contribute substantially to underestimating the magnitude and duration of an epidemic and confuse assessment of mitigation strategies.

The report also assumes that the laboratory diagnostic sensitivity and specificity values are 1.0. Those are distinct from the aforementioned clinical and contact tracing sensitivity. The assumption of perfection indicates that submitted specimens from truly infected animals would test positive every time, and that specimens from truly uninfected animals would test negative every time. That is not the case in reality when laboratory assays are compared (King et al., 2006; Tam et al., 2009). For some serotypes, such as those designated as the South African Territories serotypes (SAT1, SAT2, and SAT3), laboratory test sensitivity can be quite low. Even so, published values are probably much higher than what would be experienced in practice during an epidemic because they represent testing of tissue cultures with high titers of virus rather than testing of clinical samples that may have virus titers that are several orders of magnitude lower, which would consequently be more likely to result in false-negative results.

The consequence of those inherent diagnostic assumptions would be that the model would incorrectly assume that all infected herds would be identified and declared with clinical

and contact tracing and investigations and then confirmed by laboratory testing. Because a percentage of infected herds would be missed in a real outbreak, the model has underestimated the number of cases and the duration of the epidemic. Delays in diagnostic testing resulting from loss of the NBAF diagnostic capability could result in continued spread of disease while awaiting orders to cull the animals of suspected positive herds.

Initial Cases of Fomite Leaks Restricted to Manhattan, Kansas, Area

As part of efforts to prevent FMD from entering the United States, the U.S. Department of Agriculture has established programs that prohibit travelers from carrying certain animal products that are potentially contaminated with FMDv into the United States, and it has specific inspection procedures at ports of entry to enforce the requirements. It is unclear, therefore, why a seemingly likely scenario was not considered for an FMDv fomite "walking out" of the NBAF via a person who became contaminated with the virus in the laboratory and who flew or drove from Manhattan, Kansas, to a livestock or wildlife site in some other state. The assumption that the first case of FMD resulting from fomite escape from the NBAF would appear only in the Manhattan area (pages 168-169) ignores the reality of human travel and disease movement, especially in a university town. By not including a scenario of escape to another state, the model allows the disease to be diagnosed and controlled only in a very small area around Manhattan that presumably has been bolstered, because of the presence of the NBAF, with an unusually high degree of passive surveillance and education, which would be expected to provide earlier detection and control than would occur in other states. Consequently, model results will be biased toward a low estimate of magnitude and duration of an FMD epidemic in the seven states studied.

Additional Concerns about the Model

The committee questioned the following aspects used in the model:

1. The ability to cull and bury or burn animals from 120 infected premises and to destroy all feed and clean and disinfect environments of these premises in only 1 day is too optimistic even if military intervention is involved.
2. No indication was provided as to whether contiguous cull was considered in the model.
3. No indication was provided as to specific vaccination strategies that were considered, how populations were selected for vaccination, and specific timeframes (and limits to the estimates).
4. An assumption inherent in the scenarios presented was that only one strain of one serotype of FMDv would be released. That assumption would not represent the situation if the laboratory were physically breached (by airplane, tornado, or other damage) or if filtration systems failed, given the presence of many strains of all seven serotypes of the virus in the laboratory. The model also assumes that none of the leaked strains would be cell or tissue-culture-adapted; if they were, that could result in different disease manifestations than those modeled. For example, infection with engineered or adapted strains, such as the one that escaped into Taiwan swine (Beard and Mason, 2000) might not be manifested in typical clinical signs expected for FMD or might not be detected by PCR testing, thus delaying detection and perhaps control. Several other scenarios could

Rift Valley Fever

In the preliminary letter report, the committee advised DHS to include in the SSRA a pathogen that posed a potential risk to humans. DHS subsequently chose to investigate the potential risks posed by research on the Rift Valley fever virus (RVFV), which is a BSL-3 pathogen that will be studied at the NBAF.

To conduct quantitative studies of the risks posed by a release of RVFV, the SSRA team developed a new, custom epidemic model, using the VenSim software package. FMD has been the focus of numerous modeling studies, but Rift Valley Fever (RVF) has not received similar attention. There were no suitable models of the quality of the NAADSM or the Davis Animal Disease Simulation (DADS) models for addressing community risk posed by a release of RVFV. Without a suitable existing model, the only available course for meeting the requirements of the SSRA was the development of a custom model, as described in Section 4.4 of the SSRA.

The SSRA RVF epidemic model is a compartmental model that represents transmission dynamics between vertebrate hosts and mosquitoes, the arthropod vector responsible for RVF transmission in the wild. It includes parameters representing the course of infection in vertebrates and mosquitoes, biting rates, mosquito lifetimes, and some potential mitigation measures, but it does not incorporate spatial or geographic structure. Values were assigned to the parameters by using data from a variety of sources, and the SSRA specifically identifies some kinds of data that are absent and for which further basic research is needed.

The RVF model is described in detail in the SSRA (pages 237-243), but in lay language. Although the model described in lay language seems reasonable and appropriate, its implementation remains opaque. The lay language is imprecise, making the independent replication of the model difficult. The algorithms used by the VenSim software package for simulating the model are not described; therefore, it is unclear what form the model takes (such as ordinary differential equations, stochastic differential equations, birth-death process, and individual-based simulation). Because the model is new, there has not been much opportunity for it to undergo peer review and independent validation, which would address those issues. In addition, the absence of basic research in some areas leaves large gaps in the model parameterization that are important in assessing the overall effect of an RVF outbreak. Even some aspects of the model that have been extensively studied, such as mosquito biting rates, still have substantial uncertainty.

In addition, the RVF model in the SSRA assumed that the only infection mechanism in humans was primarily by mosquitoes and possibly by biting flies as well. The current view on risk factors for infection with RVF in humans is that direct contact with animals, particularly contact with body fluids, is one of the most important risk factors (Woods et al., 2002). In a country such as the United States, the consequences of such transmission routes create considerable uncertainties with respect to the risk of infection in the human population.

Collectively, the issues noted above leave the committee with no confidence in the quantitative results of the SSRA's RVF epidemic model. The issues also limit the committee's confidence in the analysis of the economic consequences of an RVF outbreak to the extent that it depends on the epidemiological model. Numerical results obtained from simulations of the

SSRA's RVF model should be treated as guesses and should not be relied on in assessment of risk or in the design of mitigation measures. The omission of direct transmission may significantly bias results. The RVF model does provide constructive content for the SSRA to the extent that it partially identifies factors—some known and others for which more will need to be known—that could contribute to the potential spread of an RVF outbreak. The identified factors provide qualitative guidance for potential risk pathways that require further attention and research as part of continuing risk assessment and mitigation practices.

The committee expects that the development of an RVF model comparable with the NAADSM or DADS would require a year or more of work, and it may not be possible to complete and calibrate an RVF model without further epidemiological research. The committee acknowledges that the time frame given to DHS for conducting the SSRA was shorter than the time needed to further develop the model for assessing the risk of RVF.

ECONOMIC MODELING

The evaluation of the economic modeling portion of the SSRA is based on the revisions to Chapter 5 of the SSRA that were submitted to the committee on August 26, 2010. The report has several positive aspects, especially the integration of epidemiological modeling with economic modeling. Three economic models are used in concert with cost calculations external to the modeling.

Methods Employed

A partial equilibrium model of the U.S. agriculture sector, also referred to as an equilibrium displacement model, is used to estimate the national effects of FMD and RVF outbreaks. Such models estimate prices, quantities, and economic welfare in the United States in an open international trading system. The model used is documented as cited in the SSRA but is modified with more recent elasticity estimates.

The SSRA correctly used the partial equilibrium U.S. agricultural sector model by considering the effects of three shocks caused by an outbreak. One shock is the reduction in the supply of animals determined by the epidemiological model discussed. The number of animals culled are reported in Table 5-5 of the SSRA and are converted to percent reductions compared to the U.S. inventory as shown in Table 5-10 of the SSRA. A second shock is a reduction in U.S. exports of meats and animals that is assumed on the basis of World Organisation for Animal Health (OIE) guidelines, observed experiences in other nations that have FMD and RVF, and the U.S. bovine spongiform encephalopathy (BSE) event. The assumed export reduction used in the SSRA is plausible: the SSRA analysis assumes U.S. exports of relevant products drop by 95% during the outbreak and the first quarter following the end of the outbreak. The 95% reduction reflects that the United States could export some cooked products. Export recovery occurs slowly over 9 quarters after the United States recovers its FMD-free status. The quarter-by-quarter percent reductions are shown in Table 5-15 of the SSRA, and these reductions are a substantial source of the economic losses. The December 2003 case of BSE resulted in reduced U.S. beef exports by 93% (USITC, 2009). Assuming there was no growth in U.S. beef exports, export quantity did not approach pre-BSE levels until the third quarter of 2008 (USITC, 2009). That pattern occurred even though Japan and Korea had earlier relaxed, but not ended, restrictions on

purchases of U.S. beef (USITC, 2009). The third shock is a potential reduction in U.S. consumption of meat and dairy products. Table 5-13 of the SSRA assumes reductions in consumer demand, and shows the largest reductions (of 5-10%) during the outbreak and a gradual recovery afterwards. The assumed reduction in demand is also based on observations of other nations and statistical estimates after the U.S. BSE cases. During the first month after the 2003 BSE case, sales decline was 21% (Schlenker and Villas-Boas, 2009). By day 90, the estimated sales reduction was 10% (Schlenker and Villas-Boas, 2009). Using the regression model of Schlenker and Villas-Boas (2009), consumer demand for U.S. beef appears to recover around day 150. The SSRA's partial equilibrium U.S. agricultural sector model is an appropriate modeling framework, and the model has been used to estimate the national impacts of other livestock diseases. The values of the three shocks are reported in the SSRA.

The second model is a regional input-output model constructed from the input-output model developed by the Bureau of Economic Analysis. Regional input-output modeling is an accepted means of estimating the economic impact of a localized shock. Typically, regional input-output modeling holds prices and costs constant because they are determined in national or global markets. The value of economic activity is changed to track its effects. Regional analysis relies on multipliers, and these can be different from the measures used in the partial equilibrium model. The partial equilibrium model treats prices as endogenously determined in global markets, so it becomes a means of recognizing price effects resulting from disease outbreaks. The economic estimates from the regional input-output model need to be compatible to be added to the estimates from the partial equilibrium model, as was done in the report. The report indicates that the regional effects are modified to avoid double counting of the impacts obtained with the partial equilibrium model. It does not report detailed sector impacts.

The third model used in the economic analysis provides estimates of values attached to mortality and morbidity that result from an outbreak of RVF. The report generates estimates of marginal willingness to pay (WTP) to avoid RVF by using questions about vaccination options to elicit survey responses and using a value for a life updated from other estimates. Those techniques are often used to determine the value of non-market attributes, such as environmental amenities and disasters, recreation, and public goods. The methods have several problems in application. The SSRA recognizes the problems and discusses them.

In addition to the three models, various costs are relevant to a disease outbreak that are external to the partial equilibrium and input-output models, such as quarantine, surveillance, destruction, and carcass disposal. It is correct to include such costs. Estimated values used in the analysis are taken from values reported in other studies.

Concerns about Implementation of the Analysis

Although the models are appropriate, the quality of the results depends on how the models are used. The estimated impacts from the partial equilibrium model are generated from the shocks introduced into that model and its parameter values. Except for the livestock products price elasticities, the parameter values are documented in the report cited in the SSRA; the price elasticity estimates for livestock products are from more recent published research. Although it is unknown what will occur in reality, the reductions in export and domestic demand are assumed on the basis of evidence cited in the SSRA. The values assumed are plausible and can be defended. The livestock depopulation and outbreak duration used in the partial equilibrium model are from the epidemiological model. As indicated above, the committee believes that the

magnitudes of livestock culls and the durations of outbreaks are underestimated. The estimated livestock depopulation ranges from 94,000 head to 23 million head in a susceptible population in the epidemiological model's database of 61.9 million head. The longest estimated duration of an outbreak is no longer than 2 quarters (6 months); the 2001 outbreak in Britain lasted from the last week of February through the end of September (UK-MAFF, 2002), and about 6 million head were culled during that 7-month outbreak (UK-Defra, 2004). Export and domestic demand recovery times depend on the duration; OIE guidelines state that a nation can recover its FMD-free status 3-6 months after the end of an outbreak, depending on how the outbreak is managed (OIE, 2009).

The same concern applies to the regional analysis and the government cost calculations. Both estimates are contingent on the magnitude of livestock depopulation and the duration of the outbreak. Many of the government costs are herd-based, so the size and number of herds depopulated affect the scale. Greater depopulation of animal numbers and herds would raise the costs. These economic effects are calculated only for outbreak duration, and longer durations would increase the effects. The SSRA description of how the regional analysis is conducted is inadequate in the text and leaves the reader to assume that it was done correctly unless proven otherwise. The specific shock introduced into the regional input-output model is not reported. The total dollar regional impact of each scenario is reported, but results for individual economic activities that would help to confirm the quality of the analysis are not reported.

The SSRA recognizes the problems inherent in WTP estimates and describes steps undertaken to mitigate them. Comparisons with similar values from research on diseases other than RVF are used to validate the results. Because the values are unknown, it is difficult to determine the success of the efforts beyond noting that the proper methods were applied.

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4

Evaluation of Design Plans and Personnel Preparedness

FACILITY DESIGN FOR BIOSAFETY AND BIOSECURITY

Facility-related design guidelines for high-containment laboratories have been developed to reduce the potential for escape of human and animal pathogens due to mechanical failure, to ensure that rooms that house animals maintain environmental parameters, and to enable continuity of operations (AS/NZS, 2002; USDA-ARS, 2002; Public Health Agency of Canada, 2004; Mani and Langevin, 2006; UK-HSE, 2006; CDC, 2009). These design guidelines collectively and in most cases independently identify the requirement for reliable systems that have been demonstrated to be capable of maintaining containment, and they identify the need for monitoring by the engineering staff and users to ensure that systems function in accordance with their design and intended functions. These guidelines also identify inherent challenges associated with engineering components, including the need for maintenance (which requires shutdown of systems), instances of malfunction and repair, and the physical limitations of systems. To reduce risks of biocontainment failure associated with failure of engineering components—such as high-efficiency particulate air (HEPA) filters; waste-effluent treatment systems; autoclaves; heating, ventilation, and air-conditioning (HVAC) exhaust fans; and backflow preventers—design guidelines advocate or require the use of redundant components. For example, the use of parallel filter banks would allow cleaning and decontamination of filters without the need to shut down operations.

Management of Solid and Liquid Waste

Residuals management is a paramount containment issue for the National Bio- and Agro-Defense Facility (NBAF). Residuals are defined here as bioaerosols, solid waste, liquid waste, and sanitary flows (sewage and associated wastewater) generated by NBAF operations. With respect to the immediate infrastructure for the containment, collection, and treatment of residuals generated by the NBAF's proposed laboratory and suite of operations, the committee has confidence in the experience and the ability of the civil, environmental, and architectural engineering teams to design systems that meet or exceed the specialty residual decontamination challenges for this unique facility. Such experience would include, but not be limited to, parallel design and operational practices of experimental animal facilities that have similar charters and

occupational and environmental standards for containing human infectious diseases specified in the fifth edition of *Biosafety in Microbiological and Biomedical Laboratories (BMBL)* (CDC, 2009).

Given the stage of the infrastructure pre-design presented in the site-specific risk assessment (SSRA) and U.S. Department of Homeland Security (DHS) responses to technical questions about the design and projected effectiveness of the different residuals management systems, the committee has a reasonable degree of confidence in the design and operations of the sanitary and solids handling systems. However, the committee remains unsure about the following sanitation-driven air-quality engineering issues:

- How relatively large indoor bioaerosol loads—in terms of mass, particle size distribution, and agent longevity—would differ markedly from those in biosafety level 3-4 (BSL-3/BSL-4) facilities that do not house cohorts of large animals.
- How such bioaerosol loads are likely to affect the design and operations of the associated indoor air quality systems.

DHS responded to direct technical questions 35-41 in their follow-up letter (pages 27-31, July 28, 2010). By reasonable and customary practical engineering standards, the committee agreed that the design, operation, and maintenance information provided was sufficient to judge how the sanitary infrastructure will likely perform as individual treatment processes. The projected sanitary performance has a sound basis as judged by the loads and designs of facilities that have similar charters. Also, the projected redundancies are in accordance with those of facilities that have similar charters, but need to be appropriately scaled for the projected NBAF loadings. The recent announcement of a wastewater treatment plant on the NBAF campus will need to be clearly justified and explained with respect to its service intents and mission over the design life of the NBAF.

Air Handling and Air Filtration Systems

As the NBAF progresses through the design phase, it is important that a commitment be made to not "value engineer"[1] out critical secondary containment systems in BSL-3Ag and BSL-4 spaces that will house large animals. Certain features of the large animal rooms will act as primary barriers for containment, such as HEPA exhaust filters and the sealed and pressure-tested room surfaces (USDA-ARS, 2002). At a minimum, NBAF should comply with national guidelines[2] that were developed to reduce the risk of escape of severe foreign animal pathogens,

[1]Value engineering refers to a practice where the architect and engineering firm is asked by the owner or building proponent to find elements that can be removed from designs to reduce costs. The owner weighs the risk and impact of the proposed changes against the benefit of the cost reduction to determine which elements are safe to remove so they are no longer part of the facility construction.

[2]In designing and operating modern, high-level biocontainment facilities, both the *BMBL* and the U.S. Department of Agriculture's Agricultural Research Service facility design standards strongly recommend backup HEPA filter units to allow filter changes without disrupting research (USDA-ARS, 2002; CDC, 2009). The guidelines state that "the most severe requirements for these modern, high level biocontainment facilities include *HEPA filters arranged both in series and in parallel on the exhaust side*, and parallel HEPA filters on the supply side of the HVAC systems serving 'high risk' areas where large amounts of aerosols containing BSL-3-Ag agents could be expected (e.g., large animal rooms, contaminated corridors, necropsy areas, carcass disposal facilities, etc.)" (USDA-ARS, 2002; CDC, 2009). For these high-risk BSL-3Ag and BSL-4 areas, redundant supply and exhaust fans are recommended (ref Appendix D point 6, CDC/NIH BMBL, 2007).

such as foot-and-mouth disease virus (FMDv), that can result in catastrophic economic loss, and of potentially lethal zoonotic pathogens, such as Nipah and Hendra viruses, that have medium to high lethality and for which no vaccines or treatments are available. For BSL-3Ag spaces, the guidelines strongly recommend two HEPA filters installed in series and a parallel redundant bank of HEPA filters so that one or both of the HEPA filters in the primary bank can be replaced while the room is still operational ("hot") (CDC, 2009). Replacement may be needed because of filter loading, damage that results in leakage, or other factors that may compromise filter performance.

The SSRA falls short of recognizing that BSL-3Ag areas will generate much greater concentrations of pathogens than typical laboratory-scale work because of the large animal component in BSL-3Ag areas: infected animals shed significant amounts of pathogens. Secretion and excretion from infected animals, combined with routine maintenance and cleaning of animal areas, will most likely result in a much higher potential for pathogens to aerosolize. The secreted and excreted materials will be contained in nasal, oral, fecal, and other exudates that provide a protective bioburden matrix. Upon aerosolization, the matrix droplets will likely contain higher concentrations of virus than will be seen in the research laboratory setting. Furthermore, the SSRA does not discuss or describe the effects of additional residues—such as animal hair and food residues—that may also become aerosolized by the animals themselves or by cleaning processes, each of which may shorten the life span of the HEPA filters because of loading beyond normal operational limits. The committee concludes that because of the high rate of viral shedding, high concentrations of aerosolized virus due to animal and caretaking activities, and the increased probability of filter loading, the NBAF will need to use both HEPA filters in series and redundant (i.e., parallel) systems for BSL-3E special procedure rooms and BSL-3Ag and BSL-4 spaces.

The committee is seriously concerned that the current NBAF design strategy omits a parallel redundant bank of HEPA filters for BSL-3Ag and BSL-4 animal rooms (see Figures 3-21 through 3-28 of the SSRA). The SSRA depicts the use of two HEPA filters in series for BSL-3 special procedure rooms, BSL-3Ag, and BSL-4, but it does not address the need for a redundant series of HEPA filters in case the primary bank of filters requires replacement. Something as simple as blockage of a coarse exhaust filter becomes a major issue if the room is filled with animals infected with a dangerous pathogen. Parallel systems help alleviate such problems and allow more continuous use of expensive laboratory and animal space with minimal downtime for maintenance. The decision to omit parallel redundant series of HEPA filters was made in contravention of both the *BMBL* and USDA ARS Facility Design Standards strongly recommending both HEPA filters in series and parallel redundant systems for BSL-3Ag and BLS-4 spaces. Appendix C of the SSRA states that "the [DHS-convened qualitative risk assessment subject matter expert] panel expressed concerns regarding the practicality (size, space, configuration, maintenance, costs, etc) of parallel (fully redundant) series HEPA exhaust pathway." The committee is troubled that reasons of practicality and cost-saving measures would possibly trump and compromise critical design safety measures. The SSRA's plan to omit redundant filters is not in accordance with best practices and guidelines and is an example of the type of value engineering that should not occur.

The use of select agents, including the 8 pathogens that the NBAF will study, requires registration with the CDC or USDA and compliance with the most recent *BMBL* guidelines. Furthermore, if the NBAF is intended to be a state-of-the-art high-biocontainment facility, it will need to employ state-of-the-art biocontainment designs, operations, and practices, such as the use

of HEPA filters both in series and redundant filter banks. Removing redundant HEPA filters will result in a facility whose safety engineering is not equivalent to the safety engineering found in existing biocontainment facilities, and the NBAF will fail to be considered state-of-the-art.

The committee is aware that the budget for the NBAF is congressionally approved and has been programmed years in advance of construction, and that costs of building complex biocontainment facilities tend to increase during the time required to complete construction. Point 44 of DHS's July 28, 2010 follow-up letter states that "the *BMBL* description of HEPA series and parallel requirements is indeed very severe" (page 32). The committee cannot think of many things more severe that are related to this project than the escape of foreign animal diseases in an agricultural environment such as that of Manhattan, Kansas. The redundant HEPA filters in the BSL-3E special procedure rooms and BSL-3Ag and BSL-4 areas present a necessary expense in weighing the consequence of pathogen escape from these high-biocontainment areas. In the event that Congress does not approve supplemental funding, a rational and responsible alternative to engineering out the needed safety systems, such as redundant HEPA filters, is to reduce the operational square footage of high-cost areas. An example would be to reduce the square footage of completed BSL-3Ag holding rooms by abbreviating the length of stainless steel ductwork initially installed for the HVAC and stubbing the plumbing and electrical installations that lead to the containment rooms until funding is available for completing the project. That solution has been applied to comparable containment facilities, does not compromise safety, and ensures that the facility can accommodate future increased capacity to fulfill the NBAF mission.

With respect to sanitary and air-quality infrastructure, the committee finds that the methods used to assess and predict the sanitary, solids, and bioaerosol loads are adequately presented. Given the scale and challenges associated with biocontainment in this facility and the engineering design and maintenance information presented, the committee has confidence in the projected performance and reliability of the sanitary systems and solids management systems, but does not have confidence in the projected performance of the associated air quality systems as currently designed. The design plans are still in a nascent stage, therefore committee could not assess how the individual containment and treatment systems might perform when integrated into the synchronized network, which is to maintain this facility as an immune building under its full operational load.

PERSONNEL TRAINING AND PREPAREDNESS

The SSRA indicates that the most probable cause of accidental release will be human error. Human error can be reduced by rigorous hands-on training in laboratories that will have comparable biocontainment and biosecurity practices. However, SSRA timelines do not provide for that level and extent of training and could increase the probability of an inadvertent release or human exposure.

Personnel Practices

As noted in the committee's preliminary letter report: "it would be useful to consider the risks associated with the lack of respiratory protection for workers that come into contact with FMDv. It is a common recommendation that workers exposed to FMDv-infected animals not

contact other susceptible animals for 5 days—as a result of studies demonstrating recovery of virus from nasal passages (Sellers et al., 1970, 1971)—to reduce the risk of respiratory transmission. While the committee is not aware of literature showing this as an important route of transmission, the SSRA should be thorough and also address the risk of transmission to cattle in the Manhattan, Kansas area due to the contamination of respiratory tracts of workers." The SSRA did not address those issues.

Staff and Personnel Training

Staffing and training of staff is a large subject, some of which will only be described later in the process of bringing the NBAF online. However, with regard to scientific excellence and public service, one key aspect that will contribute to the NBAF's success will be the quality of its senior staff. It is not too early to acknowledge the need to develop more detailed recruiting, retention, continuing education, and career development plans.

Given that the NBAF is in its early planning phase, it will be important to elaborate on staffing plans more than the current version of the SSRA document does, especially if human error may be the most likely hazard of concern. Whereas the SSRA estimates roughly 300 staff members in the NBAF, it does not mention site-specific risks associated with staffing. A proper assessment will need to provide much more detail about staff composition other than the numbers in each specialty laboratory, such as consideration of their experience, national disciplinary standing, reputation, expertise, and other personal qualities required for working in high-containment settings. The matter is amplified by the intent of the NBAF to work with zoonotic pathogens in large animal facilities, a new capability for the United States. The SSRA noted that human error is the most likely cause of laboratory-acquired infection or release of a pathogen (via various scenarios), so it is imperative that laboratory workers receive the best training available. The NBAF will also inevitably expand its mission to move further into the modern world of molecular virology, molecular immunology, molecular pathogenesis and pathophysiology, molecular vaccinology, and therapeutics—fields of biomedical science from which disease prevention and control strategies are to emerge.

Federal and International Regulations

It is expected that further federal regulations, guidelines, or standards are forthcoming regarding the qualification, certification, or accreditation of staff who work at BSL-3 and BSL-4 containment levels. Work with zoonotic agents at the NBAF will need to conform to biothreat agent regulations, such as the Select Agent Rule, and other future regulations regarding biothreat agents will need to be anticipated. In addition, U.S. scientists and technicians will need to be trained to conduct work that is internationally regulated by the World Organisation for Animal Health. Hence, DHS will need to outline steps that enable the NBAF to be fully equipped to handle internationally-regulated diagnostics from day one.

Subject Matter Experts

Like other world reference laboratories, the NBAF will need world-class subject matter experts to be integral in the training process. Subject matter experts are well aware of current research, developments, practices, and thinking in the international community, and such

knowledge will provide staff with a critical understanding of each disease and disease agent to be studied at the NBAF.

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5

Overall Assessment, Findings, and Concluding Remarks

The site-specific biosafety and biosecurity mitigation risk assessment (SSRA) is critical for identifying risk factors and determining what can be done to minimize the risks inherent to the proposed National Bio- and Agro-Defense Facility (NBAF), and for determining whether construction of the NBAF should proceed in Manhattan, Kansas. Assembling the data and performing the SSRA on the proposed NBAF was a large undertaking. The Department of Homeland Security (DHS) and its contractors should be commended for performing the SSRA within a remarkably short time frame.

OVERALL ASSESSMENT

The committee evaluated the SSRA's methods, facility design plans, and mitigation strategies. The committee found that the models used in performing the SSRA appear to be appropriate and that many of the SSRA's general conclusions are valid. The SSRA has considered the major release pathways (aerosols, fomites, liquid waste, and solid waste), as recommended in the committee's preliminary letter report (see Appendix B), and has addressed mitigation strategies for each. DHS has also appropriately responded to the Government Accountability Office's (GAO's) prior criticism that it had inappropriately dealt with a potential plume from an airborne release of foot-and-mouth disease virus (FMDv); the SSRA uses a state-of-the-art puff dispersion model to simulate the aerosol transport of pathogens, which turned out to be a less critical pathway of FMDv spread than the near-site exposure of cattle. However, as described in the findings below, the committee found that the SSRA had several major shortcomings with respect to potential risks and impact scenarios, and there are some critical limitations in the SSRA's execution and analysis.

The committee concludes that the SSRA has many legitimate conclusions, but the SSRA is not entirely adequate or valid. The SSRA does not account for the overall risks associated with operating the NBAF and conducting FMDv work in Manhattan, Kansas. The inputs and assumptions for the models are inadequate because they do not fully account for how a biosafety level 3 agriculture (BSL-3Ag) and BSL-4 facility working with large animals would operate, how pathogens might be released, and which animal populations might be exposed. The SSRA sometimes used arbitrary assumptions and did not account for uncertainties, some of which

require experimental data that are currently not available but that could greatly alter the outputs. Consequently, the committee is concerned about the validity of the actual risk and impact levels determined by the SSRA's outcomes from the models.

Given more time, the SSRA may have progressed further and may have better addressed some of the concerns expressed in this report. The committee thus views this as a first step in an iterative process aimed at identifying and minimizing risk and determining actions that will need to be taken.

FINDINGS

The SSRA shows that constructing the NBAF in Manhattan, Kansas, carries a number of risks and that the impact of an FMDv release could potentially have significant economic, health, and national security impacts. Some of the risks and impacts are generic to a high-containment large-animal facility, and others are specific to the Manhattan, Kansas, site. The risk of release is primarily a generic concern, whereas the risk of infection, spread, and impact is largely related to the site. The SSRA's estimates indicate that the probability of an infection resulting from a laboratory release of FMDv from the NBAF in Manhattan, Kansas approaches 70% over 50 years (see Figure 3-1) with an economic impact of $9-50 billion. The committee finds that the risks and costs could well be significantly higher than that, and elaborates on those findings below.

Finding 1: The SSRA lacks evidence to support the conclusion that the risk of release that results in infection is very low relative to the risk of infection introduced from an external source.

The SSRA states that "given the combination of proven biocontainment design and robust operation procedures and response planning, the NBAF operations in Manhattan, Kansas overall brings extremely low risk relative to the greater risk of the intentional or accidental introduction of FMDv by an external source" (page 1, SSRA follow-up letter, July 28, 2010). Although the committee affirms that engineering and operational safeguards can substantially lower the risk of release, the committee does not concur with the implied conclusion of the SSRA that there is a very low risk of release that would result in an infection. That comparison to the "risk of intentional or accidental introduction" is misleading because the SSRA does not consider or quantify the risk of FMD infection from an external source; thus, with no data for comparison, the SSRA's conclusion of "extremely low risk" is invalid.

Furthermore, the SSRA's characterization of risk as very low is inconsistent with the risk of infection presented in the SSRA's estimates over the expected lifetime of the NBAF. The SSRA did not account for the cumulative risk of a release and infection that could spread across the expected life span of the NBAF. The need to include lifetime risk estimates is consistent with the Homeland Security Presidential Directive 9 (HSPD-9) mandate to "develop a plan to provide safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases," and is also consistent with the National Research Council's previous recommendation to DHS that the agency address the probabilities of a sequence of events that would lead to a pathogen release (NRC, 2008).

Assuming that the SSRA risk estimates are credible and reliable, if the risk probabilities across all escape pathways and scenarios had been taken into account, the SSRA would have indicated that an escape of a pathogen, such as FMDv, and an ensuing disease outbreak is more likely than not to occur within the 50-year life span of the NBAF. As previously mentioned, the SSRA's estimates indicate that a release of FMDv resulting in infection outside the laboratory has a nearly 70% chance of occurring with an economic impact of $9-50 billion. Also, because the SSRA did not account for important uncertainties and risk factors as discussed below, the SSRA could well have underestimated the risk of pathogen release and transmission and its consequences. In many scenarios considered, the numbers probably represent conservative estimates of risk.

Finding 2: The SSRA overlooks some critical issues, both site-specific and non-site-specific, that could significantly elevate the risk of accidental release and spread of pathogens.

Site-Specific

Although the SSRA accounted for the role of sales barns in increasing risk due to Kansas's central location as a hub of the U.S. livestock industry, the SSRA failed to account for other site-specific factors, including:

(1) The location of the KSU College of Veterinary Medicine clinics adjacent to the NBAF, where large numbers of sick and susceptible animals are treated and where there are large numbers of transient animal patients.

(2) The movement of personnel between KSU facilities, the Biosecurity Research Institute, and the NBAF, which increases risks related to fomites and respiratory transfers.

(3) The location of the Kansas State University (KSU) football stadium in close proximity to the NBAF, which presents a large human population that potentially could be periodically exposed to a released zoonotic pathogen and that potentially could transport a released pathogen outside of the area.

Non-Site-Specific

One of the most critical scenarios that the SSRA neglected to consider is the maintenance and cleaning of BSL-3Ag and BSL-4 large animal pens; an entire room serves as the primary biocontainment envelope. Large animal pens are normally washed daily, and this would likely result in substantial aerosol formation of BSL-3Ag and BSL-4 pathogens in addition to fomites. The daily cleaning of animal pens as a potential pathway of pathogen release would result in aerosol emissions much greater than were assumed in the aerosol scenario in the SSRA. The aerosolization of dust, dander, and other solids and liquids during daily cleaning of the large animal facilities would place an exceptional burden on the high-efficiency particulate air (HEPA) filters (even with the use of pre-filters), potentially increasing the risk of virus escape through the air-handling system, which was not addressed in the SSRA. The cleaning scenario is likely to lead to significantly increased risks of infection through fomites and airborne pathways.

Finding 3: The SSRA has several methodological flaws related to dispersion modeling, tornado assessment, and epidemiological modeling. Thus the committee believes that questions remain about the validity of the overall risk estimates.

Dispersion Modeling

The execution of the SCIPUFF model to estimate risk of infection associated with exposure to airborne virus was not based on approaches described in the literature (see Cannon and Garner, 1999; Schley et al., 2009), but instead was based on an arbitrary threshold dose of 0.1 plaque forming unit for infection, which leads to uncertainties in the estimation of risk. The modeling also did not account for uncertainties in model parameters. A typical approach would have been to combine concentration calculations with livestock population maps to derive dose contours, which could be related to the probability of infection. As mentioned above, the omission of the animal pen cleaning leads to a major underestimation of the magnitude of aerosol release.

Tornado Assessment

The SSRA used a tornado risk assessment that is sensitive to user bias. The committee could not determine whether the user judgments were reasonable or optimistic and therefore could not determine whether the models underestimate the risk of a high-speed wind event, such as a tornado, and its consequences. The use of a tornado hazard model would have eliminated the need for user judgment, and would more appropriately provide information about the design basis wind speed and building envelope design.

Epidemiological Modeling

The epidemiological modeling of FMD transmission was inadequate in several respects. Many uncertainties, some of which are discussed below, were inadequately considered, so the sensitivity analyses were insufficient and many scenarios probably were overoptimistic. Some parameter values and assumptions used in the North American Animal Disease Spread Model (NAADSM) were inconsistent with what is known about epidemiological and veterinary aspects of and experience with FMD.

(1) The *scope* of spread was limited to seven states by the exclusive use of sales barns as the sources of animal movement. The scope was also limited only to cattle and swine and did not include infection of feral swine, deer, and small ruminants.
(2) The *extent of spread* did not address the critical elements of animal movement within and among states. The transportation modeling methods considered animal movement only in an indirect and superficial manner and excluded movement within and among states (as well as incursions in and out of Canada and Mexico) by individual producers and neighbors, therefore underestimating the spread.
(3) The *response* did not provide realistic assumptions regarding mitigation values of input parameters, and the values inflated prospects of surveillance, diagnosis, available manpower, depopulation rate, and movement bans (direct and indirect). Mitigation strategies did not mention how and where FMDv diagnostics, research activities, and

matching of vaccine to outbreak strain might be conducted if the NBAF had to shut down or curtail some activities because of a pathogen escape or physical damage to the facility.

In epidemiology, studies generally are evaluated on the basis of internal and external validity estimates. Internal validity estimates are related to how well a study was conducted. If any of the elements of internal validity estimates (such as study design elements as proper controls, correct statistical or modeling methods, assumptions, non-biased selection criteria, and sampling methods) are inadequate, inappropriate, or flawed, then the study lacks internal validity. Assuming acceptable internal validity, external validity estimates indicate how well and in what detail inferences about the results of the study can be drawn. For example, restricting epidemiological modeling to its effect on seven states that have large livestock populations would mean that inferences about the other 41 contiguous states (with Alaska and Hawaii excluded) cannot be drawn, so external validity would be lacking. In the SSRA, there are several such issues that raise questions of both internal and external validity.

On the basis of the information provided, the committee could not determine the input parameters used for the NAADSM and could not independently validate the results. As a result of the assumptions and methodological flaws, the committee concludes that the epidemiological results of the SSRA deflate the duration and magnitude estimates of a possible FMD epidemic.

Finding 4: The committee agrees with the SSRA's conclusion that for FMDv, long-distance plume transport will likely be less important than the near-site exposure of cattle.

Near-site exposure of cattle and other livestock are especially a concern in Kansas State University's College of Veterinary Medicine, sales barns, and the many cow-calf operations and feedlots that are within a few miles of the NBAF; beef cattle sales barns are a particular focal point for secondary transmission of FMDv in this setting. These livestock and their transport across neighboring states will serve as major factors in the spread and amplification of an FMD outbreak throughout the United States. As shown in the SSRA, the high level of animal movement and the presence of sales barns near Manhattan, Kansas, significantly increase the degree of FMD spread and its economic impact.

Finding 5: Substantial gaps in knowledge make predicting the course of an FMD outbreak very difficult, which led to weaknesses in the SSRA.

Predictions of epidemic size are only as robust as the weakest links in the model. The SSRA identified a lack of good records and data on interstate livestock transport. Whereas there is concern about the potential role of wildlife in FMD spread, there are few resources for incorporating wildlife data into the risk assessment model. Without data, there is no way to fill in the gaps and improve precision beyond the scope of expert opinion. In addition, without improvements in data quality, it remains difficult to obtain any robust forecasts of overall outbreak effects. Considering that FMD has been intensely studied since 1898, when it became the first animal disease recognized to be of virus etiology, it is sobering that knowledge of the dynamics of viral transmission (beyond immediate contact between infected animals) is still limited. Even though specific data are lacking for predicting the nature and scope of SSRA

escape scenarios, data are available on recent FMDv introductions in other countries (for example, Taiwan in 1997 and the UK in 2001), and those introductions in many ways resemble laboratory escapes inasmuch as they were "point source" epidemics; there is also the UK experience in 2007 stemming from a laboratory escape. Those FMD outbreak episodes provide valuable lessons in understanding realistic expectations for mitigation measures and disaster preparation plans for various outbreak scenarios (UK-HSE, 2007; Anderson, 2008).

Finding 6: Although the economic modeling was conducted with appropriate methods, the epidemiological estimates used as inputs to the SSRA were flawed.

The epidemiological modeling assumptions that were used in the economic assessment, such as depopulation rates and outbreak duration, were overoptimistic in their estimates. The committee questions the SSRA's assumption that its proposed mitigation strategy would contain the spread of FMD by culling 120-720 herds per day (page 230 of the SSRA). The committee does not think that infected herds could be detected and culled at that rate, and therefore questions the validity of the mitigation strategy to limit the effects of an outbreak. If fewer herds could be culled each day, the spread and impact would be much higher than indicated by the SSRA. Consequently, the use of flawed epidemiological inputs resulted in economic estimates that were also flawed and invalid, albeit derived in a methodologically sound manner.

Finding 7: The committee agrees with the SSRA's conclusion that early detection and rapid response can limit the impact of an FMDv release from the NBAF, but is concerned that the SSRA does not describe how the NBAF could rapidly detect such a release.

Early detection is critical for limiting the spread of infection, therefore it will be important to develop extensive real-time surveillance for FMDv and other pathogens being worked on at the NBAF before the laboratory becomes operational. Surveillance will also be critical in detecting whether a leak or spill has occurred within the NBAF so that steps can be taken to minimize and mitigate its release. To implement FMD surveillance and response, it would be necessary for a number of things to occur that were not described in the SSRA, including:

(1) *Development and testing of adequate real-time diagnostic capabilities for FMDv*. These include animal-side assays that could be used in the field and ensure that all U.S. state and regional laboratories have adequate access to these capabilities so that real-time surveillance for FMDv can be conducted in the United States.

(2) *Development of real-time global full-length genomic surveillance for FMDv*. This would include:

- Developing capacity for full-genome sequencing of all FMDv isolates of interest.
- Developing the software systems needed for rapid, comprehensive analysis of genomic data.
- Maintaining a full-sequence database of all FMDv isolates in order to facilitate rapid matching of an escaped outbreak strain to the range of possible vaccine strains.
- Developing the information-technology system needed for making such data broadly available to outbreak investigation, mitigation, and forensic officials.

(3) *Development of a real-time active surveillance system*[1] *for FMDv in the United States*. This will include involving state and regional diagnostic laboratories, industry, and veterinary practitioners.

(4) *Development and testing (through modeling) methods and scenarios for surveillance, control, eradication, vaccination, and mitigation of FMD in the United States*. This would include:

- Operating an emergency response model that uses continuous meteorological monitoring equipment at the NBAF site and meteorological forecasts to provide real-time information on transport of aerosols (FMDv) released from the NBAF.
- Ensuring that the U.S. Northern Command (NorthCom) is formally engaged in developing plans for military assistance in the event of an FMD epidemic.
- Creating a plan in consultation with all appropriate federal, state, tribal, and private-sector agencies and groups to rapidly detect and control an FMD outbreak in the United States (the use of vaccine as well as traditional "stamping-out" approaches will need to be considered).
- Requiring mandatory education and training of food-animal veterinarians in FMD diagnosis, control, and eradication through the U.S. Department of Agriculture (USDA) National Veterinary Accreditation Program as a component of developing an FMD surveillance system.
- Developing contingency plans for backup diagnostic, research, and forensic laboratory services in case the NBAF is rendered nonoperational or cannot work with FMDv due to a release.

Finding 8: The SSRA lacks a comprehensive mitigation strategy developed with stakeholder input for addressing major issues related to a pathogen release. The mitigation strategies that are provided do not realistically demonstrate current or foreseen capacity for how federal, state, and local authorities would effectively respond to and control a pathogen release.

Human Health

The committee is concerned about the lack of clinical isolation facilities and world-class infectious disease clinicians experienced in diagnosing and treating laboratory staff or communities exposed to BSL-4 pathogens in the Manhattan, Kansas area. Given that people may become infected with some zoonotic agents that will be worked with at the NBAF, a plan is needed for rapid consultation with experts at one or more of the world-class high-containment laboratory facilities (BSL-4 laboratories). In addition, a plan is needed for transporting patients safely to a major medical center where world-class experienced clinicians are ready to care for an exposed or ill patient in the event of a laboratory-acquired infection.

Manhattan, Kansas, is not located adjacent to world-class clinical facilities with expertise in BSL-4 human infectious diseases. If a BSL-4 pathogen escapes or a laboratory worker acquires an infection with a BSL-4 pathogen, the deficiency of the Manhattan, Kansas, location

[1]Active surveillance is defined as "an active, ongoing, formal, and systematic process aimed at early detection of a specific disease or agent in a population or early prediction of elevated risk that a population will acquire an infectious disease with a pre-specified action that would follow the detection of disease" (Thurmond, 2003).

will become immediately apparent, and the consequences will not only damage the credibility of the federal agencies involved but will potentially cost human lives. The SSRA did not adequately address the mitigation of this risk. It will be crucial for a world-class facility like the NBAF to provide response plans that include world-class infectious disease clinical facilities and physicians who can properly diagnose, contain, and treat infected individuals.

Animal Health

The SSRA acknowledges that the Manhattan, Kansas, region is a hub of animal movement for the entire United States and that infected animals would be expected to move across the country and cause pockets of infection at great distances from the initial source of infection. The mitigation strategies do not address outbreaks of such magnitude.

Given that a pathogen release from the NBAF may occur despite all efforts to prevent that from occurring, it will be necessary to create realistic and credible mitigation strategies for the release of a pathogen. Conducting exercises can better inform stakeholders and responders at the local, regional, and national levels about the diseases and the relevant factors that will affect an outbreak. There is a need for a contingency plan to cover the costs of mitigation and indemnity.[2] In addition, mitigation plans will need to be thoroughly tested, evaluated, and updated on a regular basis to address the spectrum of credible scenarios.

It will be important to meaningfully involve relevant local and national experts and stakeholders in a continuous, purposeful, and committed initiative to obtain realistic and functional knowledge of the logistical and resource constraints, personnel limitations, political and legal actions, animal movement dynamics, and animal welfare issues that will arise in the face of a pathogen escape. The animal-owning public will need to be included in the planning and will need to understand the consequences of an FMDv escape. A working understanding of factors that contribute to FMD spread will need to be applied meticulously to the design and operation of the epidemic spread models, which will help to inform decision-makers about gaps in knowledge and data and would be relevant to inform policy options. It will also be necessary to have action plans for mitigation that can be tested in exercises sensitizing stakeholders and responders to what needs to be done to minimize the effects of a release of FMDv or other agent from the NBAF.

An important mitigation strategy for conducting research on FMDv and the other pathogens in the NBAF would be to ensure that the National Veterinary Stockpile (NVS) receives adequate funding to carry out its mandate in accordance with HSPD-9. DHS and USDA will need to ensure that the NVS will have the necessary vaccines, diagnostic reagents, and supplies to respond to a major outbreak of FMD, RVF, and other infectious agents studied in the NBAF as required by HSPD-9. Enhancing the capability of the local and regional emergency response community, the surveillance capability of the laboratories in the National Animal Health Laboratory Network, and the NVS will benefit U.S. agriculture and public health in the event of any incursion of foreign animal or zoonotic disease.

[2]As noted in an Institute of Medicine and National Research Council report, "private stakeholders [need to be] compensated for losses incurred as a result of public action, such as paying farmers an indemnity for culling diseased or suspected infected animals for an emerging disease" (IOM and NRC, 2009).

Finding 9: The committee agrees with the SSRA's conclusion that human error will be the most likely cause of an accidental pathogen release, and fomite carriage is the most likely way that a pathogen would escape the facility's outer biocontainment and biosecurity envelope.

Safe practices are of paramount importance given that the SSRA presents human error as the most likely source of accidental releases. To enhance safe operation and reduce the risk of human error identified in the SSRA, the committee agrees that key NBAF personnel will need adequate ongoing training, education, and evaluation of skills. Furthermore, there will need to be zero tolerance of deviations from biosafety standards and practices recommended by the Centers for Disease Control and Prevention (CDC) and USDA.

The Laboratory Operations Timeline (Figure 1-6 of the SSRA) could be significantly improved with regard to training by factoring in time and funds for key researchers and technicians to undergo 1-year internships at facilities currently operating at BSL-3Ag and BSL-4. Memoranda of agreement could be developed with a number of U.S. laboratories that have extensive expertise and similar missions (such as the CDC, the U.S. Army Medical Research Institute of Infectious Diseases, and the University of Texas Medical Branch at Galveston). Sufficient time for hands-on experience will enable trainees to work with experts in maximum biocontainment and participate in the gamut of activities mimicking those of the NBAF. Such training cannot be duplicated by attending a series of mini-courses, 1- to 2-week "mock" training courses, or learning by trial and error before the NBAF's certification for full operations. The trainees could form the core of trainers for the remainder of the NBAF staff.

There is a multi-year window of opportunity to ensure that the NBAF senior staff (such as principal scientists and super-technicians) are technologically, intellectually, scientifically, and culturally prepared on opening day and fully accredited to work at the highest biocontainment levels. As shown in Figure 1-6 of the SSRA, that needed specialized training would have to begin by the January 2014 timeframe to enable trainers to complete a 1-year internship or rotation, acclimate, and adapt procedures to the NBAF and begin training staff in May 2015. Furthermore, it would be of great advantage if all NBAF senior staff were hired by 2012 and provided 2-year fellowships at a national laboratory where training in biosafety and biosecurity are integrated with modern microbiological research, development, and diagnostics.

Finding 10: The committee agrees with the SSRA's conclusion that investment in biosafety and biosecurity engineering and the training of personnel and responders can reduce the risks, but is concerned about current design plans that potentially compromise safety measures.

Given that the SSRA states that the cost of a release (such as a release of FMDv) would be very high, the facility will need to be engineered beyond the accepted standards to an exceptionally high level of biosafety and biosecurity. To function safely, it will need to be a state-of-the-art facility with state-of-the-art equipment and state-of-the-art biosafety practices. Any facility design compromises due to budgetary limitations will need to be viewed as inconsistent with the mission of providing a state-of-the-art facility with minimal risk of pathogen escape from containment. Once construction of the NBAF is complete regardless of the location, funding will need to be maintained to assure continued safe operation and maintenance.

The NBAF will venture into a new and unprecedented area of BSL laboratory operations with respect to its mainland location, scale of operations, and scope of agents. It would therefore be prudent not only to abide by the strongly recommended guidelines set forth in the most recent *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, but to also glean best practices and guidance from existing BSL-4 laboratories. Doing so would inform the NBAF on BSL-4 laboratory designs, operating practices, and training and could be used as a basis for improving and establishing standards that would be appropriate for work in the NBAF's BSL-3, BSL-3Ag, and BSL-4 large animal facilities.

As the facility is still in the early design phases, the architectural and engineering firms will need to make sure they do not compromise community public health or agricultural safety and security. As previously mentioned, the committee is seriously concerned about the SSRA's current designs omitting redundant HEPA filters for reasons of practicality and cost-savings. The *BMBL* strongly advocates a redundant series of HEPA filters for extremely high-risk areas such as BSL-3Ag spaces; the NBAF qualifies as such extreme high-risk with its proposed BSL-3Ag areas and its new BSL-4 capability for large animal research. The proposed design omitting redundant HEPA filters will need to undergo review and approval by both USDA and CDC in the context of a detailed agent- and procedure-specific risk assessment (including but not limited to FMDv, Hendra virus, and Nipah virus).

It is still too early in the design process for the committee to verify and predict the infrastructure's capability for biocontainment. As the progress and specific installation and implementation of sanitary and HVAC designs mature, the NBAF management will need to assure mechanisms exist for continued engagement of professional engineers and qualified consultants who have proven skills in high-biocontainment design and operation. The critical engineering and construction plans will affect the containment potential for the life span of the facility.

Finding 11: The SSRA's qualitative risk assessment of work with BSL-4 pathogens in large animals was inadequate.

The qualitative risk assessment was inadequate because it failed to fully consider the characteristics of the pathogens and the risks of working with BSL-4 pathogens in large animal facilities. The committee does not concur with the SSRA's finding that its quantitative risk assessment regarding FMDv and Rift Valley fever virus (RVFV) sufficiently represents the range of risk regarding the other pathogens that will be studied at the NBAF, that is, the pathogens that are included in the qualitative risk assessment. The committee does not agree that the BSL-3 quantitative risk assessment adequately frames the risks associated with operating a BSL-4 large animal facility, because it is insufficient to use BSL-3 pathogens to predict risks associated with BSL-4 pathogens that are zoonotic and for which no treatment is available. Given that the qualitative risk assessment was inadequate and that the SSRA did not perform a quantitative risk assessment for BSL-4 agents, further evaluation of risks and mitigation strategies will need to be established for BSL-4 agents (for example, Nipah and Hendra viruses or other emerging BSL-4 zoonotic pathogens) to identify ways of minimizing the risks associated with working with those agents in a large animal facility setting.

There is a need to develop strong working relationships with the CDC, USAMRIID, USDA, and National Institutes of Health to understand how the NBAF can work safely with

dangerous zoonotic pathogens in large animals. There is a need for interdisciplinary research and programmatic workshops that cross traditional agency boundaries. Such interagency working relationships are often pragmatically difficult, but they are essential for minimizing risks and putting in place mitigation strategies that can minimize the effects of a release from the NBAF.

CONCLUDING REMARKS

The SSRA team should be applauded for its effort in conducting an extensive risk assessment in such a short period of time. Although the committee's findings express major concerns about the validity of some of the SSRA's conclusions, the work that was completed constitutes a huge step forward compared with previous risk assessments of its kind and should be viewed as a solid starting point.

The nation clearly needs an institution to support comprehensive research programs for the study of foreign animal and zoonotic diseases, including detection, diagnosis, and means of mitigation (drugs, vaccines, and genomic forensics). Such activities require a capability to work with all known threat agents (not just the eight infectious agents listed in the SSRA), multiple pathogen introductions, and emerging and unknown disease threats. For these reasons, the committee agrees that there is a need for a facility like the NBAF to be constructed and operated in the United States.

Constructing a BSL-3Ag and BSL-4 facility of the magnitude planned for the NBAF, one that is capable of large animal work on a scale greater than other high-containment laboratories, undoubtedly presents new and unknown risks that could not be accounted for in the SSRA because of a lack of data and experience. Given the constraints of the design framework and the short timeframe available for data collection and analysis, the committee finds that the limitations of the data, facility design details, and operating practices may have limited the scope that the SSRA could adequately address at this time. As more data, facility designs, and operational plans emerge, updated analyses may be appropriate to better evaluate the risks posed by a BSL-3Ag and BSL-4 large animal facility in Manhattan, Kansas.

The SSRA and the committee identify some sources of risk that can be addressed as part of the design, preparation, and long-term operation of the NBAF to reduce risk wherever it is located. Though the SSRA and the committee offer several points for consideration to reduce the risk of a pathogen release and its consequences, further risk analysis is needed to determine the extent to which these measures would reduce risk. Ultimately, policymakers will need to decide whether the risks are acceptable related to constructing and operating the NBAF in Manhattan, Kansas, and DHS will need to determine steps to minimize risk and impact if construction and operation should proceed as planned.

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Appendixes

Appendix A

Committee Biosketches

Ronald M. Atlas (*Chair)* is professor of biology and co-director of the Center for Health Hazards Preparedness at the University of Louisville. He received his B.S. in biology from the State University at Stony Brook and his M.S. and Ph.D. in microbiology from Rutgers University. He was a postdoctoral fellow at the Jet Propulsion Laboratory, where he worked on Mars life detection. He has served as a member of the Department of Homeland Security's Science and Technology Advisory Committee, the National Aeronautics and Space Administration's Planetary Protection Board, the Federal Bureau of Investigation's Scientific Working Group on Bioforensics, and the National Institutes of Health's Recombinant DNA Advisory Committee. He has been president of the American Society for Microbiology (ASM) and is co-chair of the ASM Biodefense Committee. His early research focused on oil spills, and he discovered bioremediation as part of his doctoral studies. He later turned to the molecular detection of pathogens in the environment, which forms the basis of biosensors to detect biothreat agents. Dr. Atlas has authored nearly 300 manuscripts and 20 books. He is a fellow of the American Academy of Microbiology and has received the ASM Award for Applied and Environmental Microbiology, the ASM Founders Award, the Edmund Youde Lectureship Award in Hong Kong, and an honorary doctorate from the University of Guelph. He often advises the U.S. government on policy issues related to the deterrence of bioterrorism.

Thomas W. Armstrong retired in 2008 from his position as senior scientific associate in the Exposure Sciences Group of ExxonMobil Biomedical Sciences, Inc., where he had worked since 1989. Dr. Armstrong also worked with the University of Colorado Health Sciences Center as the lead investigator on exposure assessment for epidemiological investigations of potentially benzene-related or other occupational exposure-related hematopoietic diseases in Shanghai, China. Dr. Armstrong spent 9 years working for the Linde Group as the manager of loss control in the gases division and as a manager of safety and industrial hygiene. He conducted research on quantitative risk-assessment models for inhalation exposure to *Legionella* and remains professionally active on that topic. He has recently contributed to publications on mathematical models to estimate exposures to hazardous materials and methods of exposure reconstruction. He was a member of the Society for Risk Analysis and remains an active member of the American Industrial Hygiene Association. The American Board of Industrial Hygiene has certified him as an Industrial Hygienist. Dr. Armstrong has an M.S. in environmental health and a Ph.D. in environmental engineering from Drexel University.

Michael S. Ascher is a graduate of Dartmouth and Harvard Medical Schools and was trained in internal medicine, infectious diseases, and immunology at Bellevue Hospital Center in New York City. He has 30 years of experience in a variety of environments, including basic and clinical research on biothreat diseases in the Army, research and practice in infectious disease and academic medicine at the University of California (UC), Irvine, and laboratory and epidemiological practice and research in the state of California public health laboratory. From 2001 to 2003, he served as laboratory consultant to the secretary of health and human services and later in the U.S. Department of Homeland Security. From 2003 to 2007, he worked at Lawrence Livermore National Laboratory (LLNL) on host-response biomarkers of infection. In October 2007, he retired from LLNL; he now works part-time at the UC Davis School of Veterinary Medicine on the BioPortal information-sharing infrastructure focused on global foot-and-mouth disease surveillance. He served on the National Research Council Committee on Biological Threats to Agricultural Plants and Animals. He serves as the senior medical adviser to the California Emergency Management Agency. He has over 100 publications.

Mark T. Hernandez is a professor in the Department of Civil, Environmental, and Architectural Engineering at the University of Colorado at Boulder. His research interests lie at the cusp of molecular biology and civil engineering, focusing on the characterization and control of biological air pollution, both natural and anthropogenic. Recent work has focused on engineering disinfection systems for airborne bacteria and viruses and on tracking bioaerosols through natural weather patterns and catastrophic events (such as Hurricane Katrina). He is a registered professional civil engineer and an active technical consultant in the commercial waste-treatment and industrial hygiene sectors. Dr. Hernandez serves as an editor of *Aerosol Science and Technology* and is the director of the Colorado Diversity Initiative. Dr. Hernandez received his Ph.D. (1992) and M.S. (1988) in environmental engineering and his B.S. (1986) in civil engineering from the University of California, Berkeley.

Barbara Johnson is president of the consulting company Barbara Johnson & Associates, LLC. She is a registered biosafety professional and has over 15 years of experience in the U.S. government in biosafety, biocontainment, and biosecurity. She has managed the design, construction, and commissioning of a biosafety level 3 (BSL-3) aerosol pathogen test facility and launched the U.S. government's first chemical and biological counterterrorism training facility. Her research includes biological risk assessment and mitigation, testing of the efficiency of respiratory protective devices, and testing of novel methods of decontamination against biological threat agents. In the private sector, she pioneered the development of the first joint biosafety and biosecurity programs between the United States and the former Soviet Union. Dr. Johnson has served as the president of the American Biological Safety Association and is coeditor of *Applied Biosafety*. She serves on the National Research Council committee that provides continuing assistance to the National Institutes of Health on preparation of risk assessments for the Boston University National Emerging Infectious Diseases Laboratory. Dr. Johnson received her PhD in microbiology.

Brendan McCluskey was appointed the executive director of the Office of Emergency Management and Occupational Health and Safety at the University of Medicine and Dentistry of New Jersey (UMDNJ) in 2006 and directs security for the university's BSL-3 laboratories. He had previously been deputy director of the Center for BioDefense (2001–2004) and acting director of the Chemical, Biological, Radiological, Nuclear, and Explosive Center for Training and Research (2004–2006) at the university. He has served as a member of the Governor's Task Force on Campus Safety (New Jersey) since 2007. Mr. McCluskey is a Certified Emergency Manager and serves as chair of the Universities and Colleges Caucus of the International Association of Emergency Managers. In 2002, he was appointed an assistant professor in the Graduate School of Biomedical Sciences at UMDNJ, where he teaches courses in bioterrorism, weapons of mass destruction, and homeland security. Until 2009, Mr. McCluskey was also an assistant professor at Kean University, where he taught courses in public administration, bioterrorism, and public-health policy. Mr. McCluskey received his J.D. (2006) from Rutgers University School of Law and his M.P.A. (2001) and B.A. (1997) in biology from Kean University.

Kishor C. Mehta is the P.W. Horn Professor of Civil Engineering at Texas Tech University (TTU). He is recognized nationally and internationally as an authority in wind loads on structures and wind engineering. He has devoted the last 38 years of his professional career to teaching, conducting research, offering short courses and seminars, and consulting for problems related to wind loads. Dr. Mehta served as director of the 10-year-long National Science Foundation–funded Cooperative Program on Wind Engineering (with Colorado State University) and the National Institute of Standards and Technology–TTU Cooperative Program Windstorm Mitigation Initiative. As chairman of the task committee on wind loads of the American National Standards Institute (ANSI) Committee A58 and of the American Society of Civil Engineers (ASCE) Committee ASCE 7, he played a major role in the development of the wind-load provisions of ANSI A58.1-1982, ASCE 7-88, and ASCE 7-95. He is an elected member of the National Academy of Engineering and a Distinguished Member of ASCE. Dr. Mehta received his B.S.E. (1957) and M.S.E. (1958) in civil engineering from the University of Michigan and his Ph.D. (1965) in civil engineering from the University of Texas, Austin.

Frederick A. Murphy is professor of pathology and McLaughlin Professor in Residence at the University of Texas Medical Branch. Previously, he was dean and Distinguished Professor of the School of Veterinary Medicine at UC Davis. His expertise is in virology, emerging and re-emerging infectious diseases, the use of nonhuman primates in infectious-diseases research, and veterinary medicine; his interests also include public-health policy and comparative medicine. Dr. Murphy is a former director of the National Center for Infectious Diseases of the Centers for Disease Control and Prevention. He is a recipient of the Presidential Rank Award and is a member of the German Academy of Natural Sciences. Dr. Murphy was elected a member of the Institute of Medicine for his research on the pathogenesis of viral disease. He is the author of nearly 500 articles. Dr. Murphy received his D.V.M. (1959) and his B.S. in bacteriology (1957) from Cornell University and his Ph.D. in comparative pathology (1964) from UC Davis.

Philip L. Paarlberg is a professor of agricultural economics at Purdue University. His research interests include the economic impacts of livestock disease outbreaks, and he is a coauthor of several articles related to the potential revenue and welfare impacts of a foot-and-mouth disease outbreak in the United States. His teaching responsibilities cover agricultural policy and international trade. He has had extensive experience from 1977 to 1985 in the U.S. Department of Agriculture (USDA) Economic Research Service (ERS), where he analyzed international trade policy issues. In 1991–1992, Dr. Paarlberg was a visiting professor at the University of Goettingen. His awards include a USDA Superior Service Award, an award for superior research from ERS, an American Agricultural Economics Association award for his PhD thesis, and an outstanding award for the journal article in 2003 from the Southern Agricultural Economics Association. Dr. Paarlberg received his Ph.D. (1983) and M.S. (1977) in agricultural economics and his B.A. (1975) in history from Purdue University.

Timothy C. Reluga is an assistant professor of mathematics and biology at Pennsylvania State University. His research focuses on the description, understanding, and prediction of the dynamics of biological systems. His core research interest is in population biology, but his work also encompasses topics in evolutionary biology, immunology, epidemiology, and computer science. His most recent work has focused on incorporating social and behavioral factors into theories of infectious-disease dynamics and management, and on using mathematical models to predict the biological and ecological transmission process of disease. He served on the National Research Council committee to review the health and safety risks of high biocontainment laboratories at Fort Detrick. Dr. Reluga received his Ph.D. (2004) in applied mathematics from the University of Washington and his B.S. (1998) in biology and mathematics from Tufts University.

James A. Roth is the Clarence Hartley Covault Distinguished Professor in the Department of Veterinary Microbiology and Preventive Medicine of the College of Veterinary Medicine of Iowa State University. He is the director of the Center for Food Security and Public Health at Iowa State University, and is also an adjunct professor in the Department of Epidemiology of the College of Public Health of the University of Iowa. Dr. Roth's research interests are in evaluating cell-mediated immunity to bovine and porcine infectious agents and vaccines, and in developing a recombinant vaccine for Nipah virus. He has testified before Congress on biosecurity preparedness and efforts to address bioterrorism. Dr. Roth serves on the National Science Advisory Board for Biosecurity and served on the Interagency Weapons of Mass Destruction Counter Measures Working Group and the White House Office of Science and Technology Policy Agroterrorism Counter Measures Blue Ribbon Panel. He is a diplomate of the American College of Veterinary Microbiologists. Dr. Roth received his Ph.D. (1981) and M.S. (1979) in veterinary microbiology and his D.V.M. (1975) from Iowa State University.

Mark C. Thurmond is professor emeritus of veterinary epidemiology in the Department of Medicine and Epidemiology of the School of Veterinary Medicine at UC Davis. He remains involved part-time as the co-director of the Center for Animal Disease Modeling and Surveillance and co-director of the FMD Surveillance and Modeling Laboratory, where he continues to pursue his research interests in infectious disease epidemiology and surveillance, particularly related to foot-and-mouth disease. His interests during the last 38 years of professional teaching, research, and service have included clinical medicine and clinical epidemiology, primarily related to infectious diseases of livestock, new methods in diagnostic epidemiology, and modeling and development of disease control and surveillance systems. Dr. Thurmond received his Ph.D. (1982) in dairy science - epidemiology from the University of Florida, and his M.P.V.M. (1975), D.V.M. (1972), and B.S. (1970) in veterinary science from UC Davis.

Akula Venkatram is a professor of mechanical engineering at the University of California, Riverside, where he has been since 1993. Dr. Venkatram's research interests include the comprehensive modeling of systems governing air quality, theoretical aspects of small-scale dispersion, the application of micrometeorology to dispersion problems, and the development of simplified models for complex systems. His research group has conducted several field studies to collect data to develop dispersion models applicable to urban areas. Dr. Venkatram has led the development of comprehensive long-range transport models, including the Acid Deposition and Oxidant Model (ADOM), the Visibility and Haze in the Western Atmosphere (VISHWA) model, and the Simplified Ozone Modelling System (SOMS). Dr. Venkatram was a member of the committee that developed AERMOD, which is the air quality model recommended by the U.S. Environmental Protection Agency for regulatory applications. Dr. Venkatram served on the Advisory Council of the South Coast Air Quality Management District (1993–1997) and was a member of the Risk Assessment Advisory Committee of the California EPA. He is the chair of the Airport Modeling Advisory Committee appointed by the Federal Aviation Administration. Dr. Venkatram is a former vice president of air sciences at ENSR Consulting and Engineering. He served as a research scientist at the Atmospheric Environment Service, Canada, for a year before joining the Ontario Ministry of the Environment, Toronto. Dr. Venkatram received his Ph.D. (1976) in mechanical engineering from Purdue University and his B.S. (1971) in mechanical engineering from the Indian Institute of Technology in Madras, India.

Appendix B

Preliminary Letter Report[1]

[1]The report that follows is the exact text of the Preliminary Letter Report provided on a privileged basis to DHS on March 26, 2010.

Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas: Preliminary Letter Report

Committee on the Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas

Board on Life Sciences
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NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This study was supported by Contract No. HSFLBP-10-C-00001 between the National Academy of Sciences and the U.S. Department of Homeland Security. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the organizations or agencies that provided support for the project.

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COMMITTEE ON THE EVALUATION OF A SITE-SPECIFIC RISK ASSESSMENT FOR THE DEPARTMENT OF HOMELAND SECURITY'S PLANNED NATIONAL BIO- AND AGRO-DEFENSE FACILITY IN MANHATTAN, KANSAS

RONALD M. ATLAS (*Chair*), Professor of Biology and Public Health and Co-director, Center for Health Preparedness, University of Louisville, Louisville, KY

THOMAS W. ARMSTRONG, Principal Investigator, TWA8HR Occupational Hygiene Consulting, LLC, Branchburg, NJ

MICHAEL S. ASCHER, Visiting Researcher, University of California, Davis

MARK T. HERNANDEZ, Professor of Environmental Engineering, University of Colorado at Boulder, Boulder, CO

BARBARA JOHNSON, Consultant for Biosafety and Biosecurity, Johnson & Associates, LLC, Herndon, VA

BRENDAN MCCLUSKEY, Executive Director, University of Medicine and Dentistry of New Jersey, Newark, NJ

KISHOR C. MEHTA, P.W. Horn Professor of Civil Engineering, Texas Technical University, Lubbock, TX

FREDERICK A. MURPHY, Professor of Pathology, University of Texas Medical Branch at Galveston, Galveston, TX

PHILIP L. PAARLBERG, Professor of Agricultural Economics, Purdue University, West Lafayette, Indiana

TIMOTHY C. RELUGA, Assistant Professor of Mathematics, Pennsylvania State University, University Park, PA

JAMES A. ROTH, Clarence Hartley Covault Distinguished Professor, Iowa State University, Ames, IA

MARK C. THURMOND, Professor Emeritus, University of California, Davis, CA

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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 process. We wish to thank the following individuals for their review of this report:

Corrie Brown, *University of Georgia, Athens, GA*
Philip Hagan, *Georgetown University, Washington, DC*
Peter B. Jahrling, *National Institutes of Health, Frederick, MD*
Jonathan Richmond, *Jonathan Richmond & Associates, Southport, NC*
Daniel L. Rock, *University of Illinois at Urbana-Champaign, Urbana, IL*
Gary Smith, *University of Pennsylvania, Philadelphia, PA*
Akula Venkatram, *University of California, Riverside, CA*
Ronald H. White, *Johns Hopkins Bloomberg School of Public Health, Baltimore, MD*
Alex Winter-Nelson, *University of Illinois at Urbana-Champaign, Urbana, IL*

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 **Roger Kasperson**, *Clark University,* and **Harley Moon**, *Iowa State 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.

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500 Fifth Street, NW
Washington, DC 20001
Phone: 202 334 2215
Fax: 202 334 1289
E-mail: bls@nas.edu

March 26, 2010

Mr. James V. Johnson
Director, Office of National Laboratories
U.S. Department of Homeland Security
Science & Technology Directorate
Washington, DC 20528

Dear Mr. Johnson:

At the request of the U.S. Congress and the Department of Homeland Security (DHS), the National Research Council's Division on Earth and Life Studies established the ad hoc Committee on the Evaluation of the Site-Specific Risk Assessment for the Planned National Bio and Agro-Defense Facility (NBAF) in Manhattan, Kansas. The committee's charge was to provide comment on the work plan for a risk assessment for the NBAF that is specific to Manhattan, Kansas location.

The committee held an in-person meeting on February 26, 2010. At the meeting, DHS staff and contractors presented their proposed approach for the risk assessment, asked the committee for specific advice on the work plan, and answered questions raised by committee members. The committee met in closed session to deliberate and draft a response to the proposed work.

This interim letter report contains the committee's responses to advise the DHS work plan for the site-specific risk assessment of the NBAF. The report contains several recommendations for consideration by the agency as it develops a more robust work plan and conducts its risk assessment for a new high-containment foreign animal disease laboratory.

On behalf of the committee, we look forward to the final report of the site specific risk assessment in June 2010 and to providing a review of that effort.

Sincerely,

Ronald M. Atlas, *Chair*
COMMITTEE ON THE EVALUATION OF THE SITE-SPECIFIC RISK ASSESSMENT FOR THE PLANNED NATIONAL BIO AND AGRO-DEFENSE FACILITY IN MANHATTAN, KANSAS

SUMMARY

The committee reviewed the U.S. Department of Homeland Security (DHS) work plan for the site-specific risk assessment (SSRA) of its planned National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas. The committee believes that the proposed work plan provides a reasonable framework but misses several fundamental issues related to the Manhattan site and the unique requirements of a foreign animal and zoonotic disease facility. The SSRA does not appropriately analyze potential pathways and will need to consider a better balance of other possible pathways of pathogen escape including, but not limited to, wastewater, fomites and residual solid wastes. The committee is concerned about the SSRA being limited to an examination of foot-and-mouth disease (FMD) and Rift Valley fever (RVF) viruses. The SSRA will need to take into account the range of risk posed by working with the comprehensive suite of pathogens that are likely to be in the NBAF, including those at the BSL-4 level. FMD and RVF viruses do not represent the array of infectivity, vectors, hosts, environmental factors, and maximum credible risk scenarios that may result from emerging pathogens with unknown characteristics that require attention in the proposed high-containment facility. The SSRA does not take into account the necessary laboratory training or management practices for establishing a competent, experienced, and credentialed workforce. Mitigation strategies are not robustly or precisely addressed and will need to include other federal, state, county, and local officials to develop preparedness and response plans. Determining the economic effects of an outbreak will require the SSRA to go beyond local market effects and include a national and international assessment that addresses additional commodities that would be affected by an outbreak. Finally, to provide a more comprehensive and thorough SSRA, DHS and its contractors will need to consult additional subject matter experts to examine all the risk factors that need to be considered.

INTRODUCTION

In its 2002 report *Countering Agricultural Bioterrorism*, a National Research Council committee identified gaps in knowledge about foreign-animal pathogens that reduced the reliability and timeliness of risk-assessment and risk-management decisions, and it determined that the ability to detect and identify some animal pathogens rapidly after introduction was inadequate (NRC, 2002). After the creation of the Department of Homeland Security (DHS), that issue was partly addressed by Homeland Security Presidential Directive 9 (HSPD-9), *Defense of United States Agriculture and Food*, which directs the secretary of agriculture and the secretary of homeland security to "develop a plan to provide safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases". To meet its obligations under HSPD-9, DHS plans to construct and operate a new facility—the National Bio- and Agro-Defense Facility (NBAF)—that, when fully operational, will replace the Plum Island Animal Disease Center ("Plum Island"). DHS has determined that Plum Island is nearing the end of its design life and lacks critical capabilities, including a modern BSL-4[1] laboratory, to continue serving effectively as the primary facility for

[1] Biosafety Level 4 (BSL-4) is the highest possible level of containment. BSL-4 laboratories are "required for work with dangerous and exotic agents that pose a high individual risk [in humans] of life-threatening disease, aerosol transmission, or related agent with unknown risk of transmission" for which vaccines or other treatments are not

research on foreign animal diseases, including zoonotic diseases. DHS also believes that Plum Island's remote location prevents effective collaboration with academic scientists.

The NBAF is envisioned as a state-of-the-art BSL-3-Ag and BSL-4 laboratory that will be capable of performing research on foreign animal and zoonotic diseases, providing a teaching facility for the recognition and management of these diseases, and providing the capability for diagnosing the highest foreign animal disease threat. One of the most serious foreign animal disease threats is foot-and-mouth disease (FMD), a disease caused by a nonhuman pathogen. FMD virus (FMDv) is easy to acquire and transmit among cattle, small ruminants, and swine; its ability to spread to limited but high-economic-value hosts poses a unique problem. Another is Rift Valley fever (RVF), which is caused by a viral zoonotic pathogen that mainly affects animals and results in substantial economic losses but also may cause severe disease in humans (BuaNews, 2010). In evaluating the risks posed by the selected site in Manhattan, Kansas, there is a need to include comparative analysis to distinguish site-specific components of risk from general components of risk that would be present at other sites.

The research agenda for the new NBAF is still unknown, but it is expected that essential and cutting-edge research will be conducted there. Such research could include synthetic biology, molecular ecology, genetic engineering, aerosol infectivity studies in BSL-3-Ag, and work with unknown or uncharacterized pathogens that may infect humans or cause latent infection in humans or animals. The NBAF is expected to permit work with large animals in a BSL-4 laboratory—a new capability that has not existed in the United States and that will carry its own unique set of risks (some which may be new) that will need to be taken into account in the site-specific risk assessment (SSRA). The NBAF research agenda will define the types of pathogens studied and the risks that they pose. It is possible to identify and mitigate risks associated with infected animals on the basis of existing knowledge, but what remains unknown is the magnitude of risk and the strategy or process flow to identify and mitigate risk in future research areas. The SSRA will need to include contingency plans that minimize risk and mitigate maximum credible risk scenarios that could result from inadvertent or deliberate release of foreign animal or zoonotic disease agents from the facility.

SELECTION OF A SITE FOR THE NATIONAL BIO- AND AGRO-DEFENSE FACILITY AND THE ENVIRONMENTAL IMPACT STATEMENT

DHS began a site-selection process for the NBAF in January 2006 and eventually selected six sites (Plum Island and five new ones) to be evaluated in an environmental impact statement (EIS). During the preparation of the EIS, DHS used Gaussian plume modeling to model the extent of FMDv dispersion in seven accident scenarios and one scenario reflecting intentional disruption for the six sites in the competition (DHS, 2008). It also analyzed the potential economic impact of an FMDv release at each of the sites. A threat risk assessment (TRA) was developed independently of the EIS to identify and evaluate potential security risks, such as crimes against people and property and threats associated with compromised or disgruntled employees. The final EIS, issued in December 2008, identified the Kansas State University (KSU) campus in Manhattan, Kansas, as the preferred site. After consideration of the TRA and the EIS, DHS formally selected a site for the NBAF in January 2009 (Federal Register,

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available (HHS, 2007). The BSL-4 portion of the planned NBAF will be designed to handle zoonotic pathogens, such as Nipah and Hendra viruses, with capabilities for large animal research.

2009). On selection of the Manhattan site, DHS planned to conduct a site-specific biosafety and biosecurity mitigation risk assessment (SSRA) to determine the requisite design and engineering controls for the NBAF; inform the development of emergency response plans with city, regional, and state officials in the event after an accidental release of a pathogen; and assist in the development of the operational protocols needed to operate the facility safely and securely.

Prior to the initiation of the planned SSRA, the Government Accountability Office (GAO) raised concerns in their July 2009 report about DHS's analyses of the risk related to performing FMD research on the U.S. mainland. The analyses were developed as a component of the earlier NBAF site-selection process. GAO faulted DHS's choice of the plume model, noting that the one used had not been validated for biological materials, and added many detailed criticisms. GAO found that DHS's economic analysis was flawed in that it focused only on the impacts of a ban on livestock exports and did not address domestic market impacts. GAO also stated that DHS did not effectively integrate the critical information from its analyses to characterize the differences in risks between mainland and island sites.

CHARGE TO THE COMMITTEE

Congressional Mandate and Statement of Task

The FY 2010 DHS Appropriation Act (P.L. 111-83) directed DHS to undertake the planned SSRA of the proposed NBAF in Manhattan, Kansas prior to the obligation of construction funds. The legislation instructed DHS to work with the National Research Council to evaluate the risk assessment and provided the statement of task shown in Box 1.

Box 1
Statement of Task

In reaction to criticism from the Government Accountability Office (GAO), the FY 2010 DHS Appropriation Act (P.L. 111-83) prohibits the obligation of funds for construction of the new National Bio- and Agro-Defense Facility (NBAF) until the Secretary of Homeland Security undertakes a site-specific biosafety and biosecurity mitigation risk assessment for the Manhattan, Kansas site. Once DHS completes the risk assessment, the Congressional language mandates that the National Academy of Sciences (NAS) provide an independent evaluation of the DHS analyses. Therefore, under the auspices of the Board on Life Sciences and the Board on Agriculture and Natural Resources, the National Research Council will convene a committee of experts to review the DHS site-specific risk assessment. The committee will not perform an independent evaluation of the safety of the NBAF, but will restrict its findings to assessing the adequacy and validity of the site-specific risk assessment.

DHS is currently conducting a source selection process for a contractor to manage the development of the risk assessment. Subsequent to the selection, the committee will undertake its first task to answer questions related to the selected contractor's work plan brought to it by DHS. In this capacity, prior to the contractor beginning their modeling and risk assessment process early in 2010, the NAS Risk Assessment Committee will meet with DHS in order to review the contractor’s Work Plan for the Risk Assessment and answer questions from DHS related to the plan. The NAS Risk Assessment Committee will convene to review the contractor’s Work Plan

and the questions provided by DHS and will provide a brief letter report to DHS in response to these questions within four weeks of this meeting. This brief letter report will not be available to the public until the second letter report of the NAS Risk Assessment Committee, described below, is available to the public. Following the delivery of the final Risk Assessment report by the performer to DHS, the committee will undertake its second task to review the finished site specific risk assessment and prepare a second and final letter report containing its findings within four months of receiving the performer's report from DHS.

The National Research Council convened a committee of experts (see Appendix A) to evaluate the SSRA of the planned NBAF in Manhattan, Kansas. In preparation for the SSRA, DHS and its contractors submitted a draft work plan for the committee to review and provided 28 written questions related to the work plan for the committee to address. The committee held its first meeting on February 25–26, 2010, in Washington, D.C. to discuss the work plan with DHS and its contractors (see Appendix C for meeting agenda). In attendance to provide presentations and clarifications about the NBAF and the SSRA were DHS and U.S. Department of Agriculture (USDA) representatives, contractors preparing the SSRA, and many subject matter experts retained by the contractors. The committee then met in closed session to evaluate the SSRA work plan and to discuss the questions raised by DHS for committee consideration. This preliminary interim letter report reflects the proposed SSRA work plan and the committee's discussions of the risk-assessment methodology.

Limitations of the Scope

In this preliminary letter report, the committee is charged with providing comments on the DHS SSRA work plan. It is not charged with comparing Manhattan, Kansas, with other possible sites. DHS conducted an EIS to provide a comparative analysis of six possible sites (DHS, 2008) and has already selected Manhattan (Federal Register, 2009). The SSRA differs from the EIS in that this risk assessment will provide a more detailed analysis of the risks, impacts, and mitigation strategies related to the Manhattan site and thus will provide finer granularity than the EIS. The SSRA is not aimed at judging whether the selection of the Manhattan site was appropriate for locating the NBAF. Instead, it will focus on the specific risks associated with the facility in Manhattan when the NBAF is constructed, on how those risks can best be mitigated (through construction design, personnel training, and laboratory protocols), and on plans for containment to minimize an impact if there is a release of a pathogen from the laboratory.

The committee's task in the second letter report will be to evaluate whether DHS has conducted an adequate and credible risk assessment of the Manhattan site. It is not in the committee's purview to interpret that assessment or to make site determinations for NBAF.

GENERAL OBSERVATIONS ABOUT THE DEPARTMENT OF HOMELAND SECURITY WORK PLAN

Without design documents and specifications, it is difficult to develop an accurate SSRA and difficult for the committee to conduct a review with confidence that the risks have been

mitigated in whole or in part by engineering and appropriate infrastructure. Nevertheless, the committee reviewed the work plan and had several overall concerns about how it was framed.

Pathways

A major emphasis of the planned SSRA has been on FMDv aerosol release and plume analyses. The committee could not discern whether the aerosol release model included consideration of nearby aerosol settling—and thus deposition on crops, grazing land, other surfaces, or animal skin—or considered only inhalation of aerosol. There are models to support the hypothesis of windborne transmission of FMDv (Gloster et al., 2005b), but previous FMDv releases provide evidence that long-distance airborne transmission may not be the main route of exposure (HSE, 2007) and that animals may be less likely to become infected through inhalation than through routes consistent with direct or indirect exposure.

The SSRA is not balanced with respect to efforts to analyze aerosol pathways compared with other potential pathways of pathogen escape. The committee recommends that the SSRA examine the release scenarios according to four categories of pathogen transport: (1) in air, (2) in solid waste, (3) in liquid waste and sanitary wastewater, and (4) in or on fomites or hosts, including workers, equipment, vectors, and dead or living animals (NRC, 2010).

The scale of the facility will present substantial sanitary engineering challenges for the safe handling and disposal of large volumes of waste—particularly wastewater and biosolids, such as feces, food, vomit, cud, fur, skin, and other animal parts—generated by its mission to handle large animals. The committee is concerned that critical aspects of sanitary residuals management have not been given appropriate attention. In the context of the SSRA, the committee recommends that additional emphasis be placed on the infrastructure for handling liquid and solid waste, the engineering design basis for management of wastewater and biosolids, and the terminal disposal plans for all residuals, including quantitative estimates.

Pathogens and Hosts

The committee is concerned about limiting the SSRA to FMD and RVF viruses. It is not clear that those two agents adequately represent the range of mechanisms of infection, vector involvement, and differences in receptors, hosts, and environmental factors likely to be present in the array of organisms to be studied at NBAF. Furthermore, FMD and RVF may not represent the maximum credible risk scenarios that may result from an emerging or unknown pathogen that may be studied in the NBAF.

DHS has indicated that the NBAF will initially work with the pathogens that cause eight diseases: FMD, classical swine fever, African swine fever, RVF, contagious bovine pleuro pneumonia, Japanese encephalitis, Nipah virus infection, and Hendra virus infection. The list of foreign animal diseases extends beyond the eight listed in the work plan; because the NBAF will be designed as a foreign animal and zoonotic disease research facility, additional foreign animal and zoonotic disease pathogens will need to be factored into the risk assessment. Whereas the full portfolio of pathogens need not be included in this SSRA, the SSRA should be broadened to consider the characteristics of all eight pathogens and other foreign animal and zoonotic disease pathogens and to address the types of unknown or emerging pathogens that the NBAF may study

in the future. A systematic enumeration of characteristics of the laboratory pathogens portfolio should be developed as part of the SSRA. This analysis should be based on a rigorous assessment and evaluation of primary scientific literature. Consideration should also be given to endemic animal diseases that are zoonotic and will have high priority for research at the NBAF and to the potential for pathogens to establish an endemic level of infection in wildlife. The SSRA should then focus on assessing the maximum credible risk scenarios related to the pathogens, including the potential impact and mitigation strategies for each scenario.

The plan for the SSRA focuses almost exclusively on BSL-3-Ag issues. FMDv is highly infectious and has great economic impact, but it is not a zoonotic agent or a BSL-4 threat. The SSRA will need to take into account the risk posed by working with a BSL-3-Ag or BSL-4 pathogen that requires special handling in the NBAF. Given that the NBAF plans include a BSL-4 laboratory with animal handling capability for large animal research, the SSRA should consider the risks related to a BSL-4 zoonotic agent that has broader host ranges than FMDv, such as Nipah or Hendra viruses or other pathogens that may be worked on in the NBAF's BSL-4 facility. The initial plan of using FMD and RVF viruses to "bracket" the severest outcomes is a reasonable start. However, biological systems are complex, and results obtained with one organism cannot necessarily be generalized to other organisms to the same extent as results in physical systems. The facility will be designed to handle BSL-4 zoonotic agents and it is likely that the laboratory will be used to the fullest extent of its design capabilities. Because of the diversity and complexity of biological systems, it is important to consider each pathogen and agent studied in the laboratory as an independent source of risk. A systematic enumeration of the characteristics of the laboratory pathogen portfolio would help identify potential risks peculiar to each pathogen. In particular, these risks may depend on the specifics of the laboratory site. In addition, such an enumeration would highlight where scientific knowledge is incomplete or uncertain so that risk-mitigation plans do not confuse uncertain risks with low risks.

In addition to known pathogens, it is reasonable to expect this laboratory to work with any emerging animal pathogens with unknown characteristics. It is important that facilities be prepared to handle risks associated with such pathogens, and that the risk assessment be sufficiently broad to address potential challenges in handling such a pathogen. However, consideration of uncharacterized emerging pathogens should be constrained to reasonably foreseeable site-specific risks and not engage in whimsical speculation.

Practices

Laboratory training and management practices will be vital in establishing a culture of biosafety and biosecurity among NBAF personnel. Those practices cannot be addressed adequately or reliably measured in a quantitative risk assessment, because they depend critically on the characteristics and ethics of laboratory personnel. Nevertheless, human factors such as training and management practices should be highlighted as critical determinants of risk. Initial and on-going training[2] is a major component of the risk preparation and mitigation process in

[2] Training is a broad term and can range from reading standard operating procedures and viewing Powerpoint presentations to having book knowledge and observing correct techniques. Training could also include a mentoring program where individuals, regardless of experience, would need to demonstrate competency while performing tasks in the laboratory. In some contexts, training is a "one time" process (such as an introduction to biosafety levels), while in other cases it may be annual refresher courses (such as courses on blood-borne pathogens and use

support of developing and maintaining an effective culture of biosafety and biosecurity among facilities personnel. The NBAF approach and commitment to training and resources should be included and described in the work plan and SSRA. The NBAF management and program will need to address how they will be able to instill and support the development of core values—bioethics, personnel reliability, and accountability—and view biosafety and biosecurity not merely as regulatory functions but as an essential part of personal and collective commitments (NRC, 2009). The challenges of attracting or developing a competent, experienced, and credentialed workforce for opening a new BSL-3-Ag and BSL-4 biocontainment facility at the Manhattan site should be addressed in the SSRA. The SSRA will also need to address mitigation of risks associated with an influx of academicians and their staff into the laboratory, which was one of DHS's justifications for locating the NBAF close to a research university.

It would be useful for the SSRA to consider the risks associated with the lack of respiratory protection for workers that come into contact with FMDv. It is a common recommendation that workers exposed to FMDv-infected animals not contact other susceptible animals for 5 days—as a result of studies demonstrating recovery of virus from nasal passages (Sellers et al., 1970, 1971)—to reduce the risk of respiratory transmission. While the committee is not aware of literature showing this as an important route of transmission, the SSRA should be thorough and also address the risk of transmission to cattle in the Manhattan, Kansas area due to the contamination of respiratory tracts of workers.

Mitigation Strategies

The work plan will need to address the mitigation strategy more robustly and more precisely than indicated in the plan for the SSRA. Cross-contamination between animals or cultures—for example, contamination of the severe acute respiratory syndrome coronavirus in a West Nile virus culture—is not uncommon (WHO, 2003), and mitigation of this type of event should be addressed. When developing mitigation, preparedness, response, and recovery plans, the mitigation strategy will also have to specifically outline the roles of DHS, USDA, and local, county, state, university, and other relevant officials throughout the project. The mitigation plan will need to address risks that are specific to the laboratory in Manhattan, Kansas, including its high density of livestock in the U.S. livestock belt, its location as a hub of livestock transportation systems that rapidly moves animals and animal products nationwide, and any risks associated with proximity to or collaboration with a university.

To understand the planned response to an FMD outbreak in the Manhattan, Kansas region, the SSRA should consult with USDA about their FMD preparedness and response plan and their draft beef cattle feedlot facility manual. Access to those draft documents can be provided by the USDA Animal and Plant Health Inspection System (APHIS) Veterinary Services (VS) National Center for Animal Health Emergency Management.

The current work plan lacks a critical component of risk communication (Reynolds, 2008) as a part of the risk-management strategy. A good risk communication strategy will need to address qualitative and quantitative risks. The public perception of risk will be influenced by the communication strategy, thus a good strategy may need to use lay language and concepts in

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of respirators) (29 CFR Parts 1910-134 and 1910-1030). When performance is critical, refresher training or competency will need to be demonstrated periodically, and the testing of learned knowledge and skills is a critical part of the training continuum.

relation to levels of risks that the general public can understand and to which they can relate, without using condescending or overly technical terms. Many of the good practices in risk communication are laid out in several sources (NRC, 1989; Sandman, 1990; Peters et al., 1997; Covello et al., 2001; CDC, 2002). These good practices and lessons from other high-containment facilities to distinguish between effective and ineffective risk communication should be applied to the NBAF SSRA (NRC, 2007, 2008, 2010).

Expertise

The committee reviewed the expertise of the DHS contractors and subject matter experts that will assist with the SSRA. The committee found that the following supplemental subject matter experts are needed:

- A sanitary and residuals engineer to address the specific pathways of pathogen entry or escape in liquid waste, wastewater, biosolids, and solid waste;
- A veterinarian who has direct laboratory and animal containment experience with FMDv, specifically in both diagnostic and research settings;
- An emergency preparedness and mitigation strategy expert who has experience in local, state, and national emergency management and response; and
- A risk communications expert familiar with the types of risks posed by a high-containment facility.

Site-Specific Analysis

The committee believes it is important to include a clear and acceptable description and treatment in the models of this site-specific risk assessment for how the geographical location of Manhattan, Kansas could affect or influence potential spread and mitigation of a disease like FMD throughout the United States.

RESPONSES TO SPECIFIC QUESTIONS POSED TO THE COMMITTEE ABOUT THE DEPARTMENT OF HOMELAND SECURITY WORK PLAN

Scenario Development

Question 1.1: Accidental scenario selection: Do these eleven accidental release scenarios sufficiently describe the range of accidental releases that adequately bound the initial conditions for plume modeling, prospective epidemiological modeling, and economic impact assessments for the Site-Specific Risk Assessment (SSRA)?

Response to 1.1: As mentioned above, the committee recommends that the release scenarios be reorganized into four main categories that correspond to fundamental paths or media for pathogen transport: (1) in air, (2) in solid waste, (3) in liquid waste and sanitary wastewater, and (4) in or on fomites or hosts, including workers, equipment, vectors, and dead or living animals. Critical path release analyses for each of the fundamental paths should include

facility engineering, personnel reliability, and operational considerations. Catastrophic events that result in multiple simultaneous avenues of release should also be considered. The committee also sees the facility as broader than just the physical place: transport of samples, the conveyances coming to the laboratory, and other activities related to the presence of the facility need to be considered. That broader context of risks associated with the facility should be considered in the SSRA.

Question 1.2. Deliberate scenario selection: Do these two deliberate/intentional release scenarios adequately represent the range of deliberate/intentional acts with enough fidelity to meet or exceed the expectations of the SSRA?

Response to 1.2: For each of the two scenarios, it would be necessary to consider insider, outsider, and *coincident*[3] threats in the vicinity (NRC, 2010).

Question 1.3. Scenario recommendations: Other than responses to previous questions, are there other accidental or deliberate scenarios or categories of scenarios that should be considered in this SSRA?

Response to 1.3: Many scenarios on the input side could be considered, but the fundamental scenarios have already been listed in the work plan. The committee believes that the risk assessment should include a transportation-specific scenario that considers the time and any risks related to transporting pathogens, for example, between the Kansas City airport and the Manhattan facility. The committee is also concerned about whether a competent workforce (from laboratorians and support staff to researchers) will be in place on day 1; the work plan should address the reality of initial start-up and personnel concerns related to operating the NBAF in Manhattan, including the transition to fully operational status and under what conditions academicians and their staff will be allowed to begin work.

It was unclear whether the work plan considered already established hazard identifications and risk assessments completed by KSU for Manhattan and the surrounding county, where some assessments dealt with similar risks but others addressed different risks. The work plan should address engaging the municipal, county, state, and university emergency management organizations; using their expertise; and considering the hazards, vulnerabilities, and risks previously identified by these entities.

Question 1.4. Approach to the development of scenarios: Will this approach to developing scenarios meet the stated purpose of the SSRA?

Response to 1.4: No. Scenario development currently excludes local responders in their mitigation strategies and responses. For an entity to be registered with USDA to work with, possess, or transfer select agents, federal law requires it to address planning and coordination with local emergency responders in its incident response plan (7 CFR Part 331). Local responders are critical components in mitigating and responding to threats, and need to be included in developing the scenarios.

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[3]*Coincident threat* is defined as a threat that becomes more probable because of a coincidental series of events (such as an occurrence with the infrastructure, procedures, or weather). For example, if there were a fire in the facility and the door locks were automatically disabled as part of life-safety requirements to facilitate emergency egress, could malevolent outsiders or insiders gain access to materials, animals, or other assets during the confusion of evacuation that they would normally not be able to access?

Signature Science, the contractor carrying out the risk assessment, noted its plans to conduct physical and virtual site visits of comparable biocontainment facilities in Geelong, Australia; Pirbright, UK; and Winnipeg, Canada. The committee agrees that it is prudent to glean best practices and lessons learned from those facilities. However, there are questions about whether the benchmarks for the other facilities will be applicable to the Manhattan site in light of site variables such as density of humans and animals (including livestock and wildlife), local climate, and infrastructure (for example, transportation and healthcare systems). One unique aspect of the Manhattan site is the high density of livestock in the vicinity of the laboratory.

The other high-containment facilities also differ in practices that may not apply to the NBAF. The Pirbright facility is aging and has infrastructure and engineering shortcomings that do not equate to the anticipated state-of-the-art design plans for the NBAF. The Geelong facility was constructed on the mainland in 1985; it does not conduct FMD research on site but instead contracts FMD research to foreign facilities (GAO, 2008). The Winnipeg facility is modern but can work with only two infected cattle at a time (GAO, 2009), whereas the NBAF potentially could work with 100 at a time. Signature Science should also consider seeking out accepted practices and lessons learned from other BSL-3, BSL-3-Ag, and BSL-4 facilities in the United States (such as the University of Texas Medical Branch at Galveston, the U.S. Army Medical Research Institute for Infection Diseases, and the Centers for Disease Control and Prevention) and abroad.

Plume Modeling

Question 2.1. Climatological datasets: Are there any other available climatological datasets that the NAS Committee would consider more appropriate for meeting the goals of this SSRA?

Response to 2.1: The committee believes the subject matter expert consultants from the National Center for Atmospheric Research listed as part of the SSRA team have the relevant expertise to recommend the appropriate climatological dataset; however, there is concern about the spatial resolution of this dataset. Whereas the climatological dataset described here may provide the best means of identifying relevant meteorological phenomena for the risk assessment, plume models of aerosol releases need to be applied on much finer time and space scales to resolve infection events. Patterns of variation may differ between the fine grid needed for plume models and the coarse grid used by climate data. The risk assessment should do as well as it can in controlling for variation among spatial scales and communicating the extent of uncertainty created by the variation. The SSRA should also explain why the puff model was chosen over other airborne-FMDv models (Gloster et al., 2010).

Question 2.2. Estimate for range of FMDv spread: Does the NAS agree/disagree with the proposed range? If NAS disagrees, what upper bound on range or parameters to determine range, would NAS recommend? Note that that this value will be used to define our computational spatial domain limits.

Responses to 2.2: There is a lack of reliable data on the parameter of FMDv's airborne transmission range and thus there is no foundation that the committee has identified in the literature for the proposed 500-km range: if FMDv could be transmitted across 500 km (for example, involving farm-related outbreaks and natural aerosol transport), FMD-free zones would not exist. The committee is not aware of any published peer-reviewed literature that can provide

an accurate basis for acceptable upper-bound limits. A study by Gloster and colleagues (2005b) suggested that if airborne transmission took place in early outbreaks, it was limited to 60 km. The article from Sørensen (2003) is used as a basis for the SSRA work plan and it proposes longer-distance spread of up to 250 km, but that range is based upon hypothetical scenarios rather than experimental data; that author also noted in the 2001 UK FMD epidemic that "long-range atmospheric disease spread was highly unlikely." The notion of possible airborne spread of FMDv was first explored retrospectively for the 1967–1968 outbreak of FMD in the UK (Hugh-Jones and Wright, 1970; Tinline, 1970). Several contemporary papers on possible FMDv transmission by wind have since been published (Sørensen et al., 2000, 2001; Mikkelsen et al., 2003; Alexandersen et al., 2003a; Gloster and Alexandersen, 2004; Gloster et al., 2005a,b, 2010; Garner et al., 2006; Sellers and Gloster, 2007; Schley et al., 2009) and should be reviewed both for estimates of parameters and for assessment of model types.

The committee suggests that a better approach to applying the estimates is needed and recommends that the SSRA ask fundamental questions about the distribution, density, and distance of susceptible animal populations around the facility. The distance to the closest susceptible animals is more critical than the maximum distance of spread through the plume model. The committee believes that cattle in near-range of the facility are likely to facilitate quicker and more distant spread of FMDv than aerosol transmission because of the various ways cattle are transported across the region and country. Therefore those transportation modes will become more relevant factors in determining the extent of disease spread, and the length of aerosol plume will become largely irrelevant.

There are several reasons for placing a more realistic and lower weight on possible windborne transmission of FMDv. A basic and critical flaw in the thinking and logical premises of those advocating windborne transmission is the assumption that because most investigations have been unable to identify with absolute certainty the contacts that led to all cases, the remaining unaccounted transmission would have been airborne. All possible means of direct and indirect contact with animals and vectors (such as birds, fox, dogs, cats, and insects) that can travel considerable distances will be difficult to quantify and examine. Early studies have pointed to the major role of weather in disease spread (Gloster et al., 2005b), and recent work has provided partial support for it; in some cases the direction of spread has coincided with or correlated with wind direction (Mikkelsen et al., 2003; Gloster et al., 2005a,b; Schley et al., 2009; Gloster et al., 2010).

The studies supporting the notion of airborne transmission have, at the onset, acknowledged their bias in favor of airborne transmission and have modeled correlation to support their hypothesis (Mikkelsen et al., 2003; Gloster et al., 2005a,b; Schley et al., 2009; Gloster et al., 2010). However, if one acknowledges the correlations found in some studies, it would be prudent to include (but not rely exclusively on) models of airborne transmission in any comprehensive approach to modeling of the spread of FMDv within the United States and to use appropriate sensitivity analyses that recognize that the amount of theoretical airborne transmission possible, if any, remains unknown. Inclusion of both direct-transmission and indirect-transmission models and airborne models would begin to address a maximum credible event scenario, a scenario that assumes airborne transmission is possible.

Question 2.3. SSRA climatological dataset validation: Are there additional SSRA validation exercises for the climatological reanalysis dataset that the NAS would recommend?

Response to 2.3: No. However, aerosol dispersal is only one of several possible modes of pathogen release from the NBAF. Recent history indicates that aerosol escape and dissemination from a laboratory that conforms to modern design and safety practices is less likely than pathogen escape through other pathways, such as waterways and fomites (HSE, 2007; GAO, 2008). Aerosol dispersal might play a role in the spread of pathogens among animals, but again it is only one of several dispersal modes and may not be the most important. Thus, the committee believes that the SSRA should initially give roughly equal weight to all potential modes of release and spread, as listed above in the four areas of general concern, and should use sensitivity analyses to assess changes in the weighting.

Question 2.4. Atmospheric fields: Are there other atmospheric fields that have a considerable impact on FMDv atmospheric transport dispersion stability and deposition, which NAS would recommend be included in our self-organizing maps analysis?

Response to 2.4: No. However, atmospheric deposition should be included as a critical dispersion factor in infective delivery (including its effect on the animal-feed supply).

Question 2.5. Climatological data reduction techniques: What other climatological data reduction techniques would NAS recommend for consideration?

Response to 2.5: None. See responses to questions 2.3 and 2.4. General parameter values used by the SSRA appear to be outdated and of little value. Several papers have published new and additional values for LD_{50}, particle size, and other factors that should be used in place of or in addition to those in the current SSRA analysis (Gloster and Alexandersen, 2004; Gloster et al., 2007, 2008, 2010; Sellers and Gloster, 2007; Schley et al., 2009).

Question 2.6. Indoor transport and dispersion models: Are there other indoor transport and dispersion models or means to estimate fire-induced temperatures and pressures that the NAS committee would consider more appropriate for this particular application?

Response to 2.6: The committee believes that there should be a better explanation of the planned role of this modeling in the overall SSRA. The chosen indoor air model assumes instantaneously well-mixed air in each chamber. That will underestimate the near-field exposure to a receptor in the same chamber. In addition, plumes can occur indoors and lead to a higher rate of initial transfer to downstream chambers. If the goal is estimating transfer and infection of another indoor receptor, more complex modeling may be applicable. However, if the goal is estimating release to the outdoor environment, the proposed model may be suitable if appropriate upper-bound estimates in the concentration range are used. The committee cautions that for a risk assessment oriented toward the environment surrounding the laboratory, conservative bounds can be derived on the basis of specific scenarios without the need for much more complex approaches; furthermore, no extra certainty would be gained.

Question 2.7. Exterior transport and dispersion models: Are there other exterior transport and dispersion models that should be considered over the Second-order Closure Integrated PUFF model (SCIPUFF) that may be more appropriate for this particular application?

Response to 2.7: At the current time, the committee believes that SCIPUFF is an appropriate engine for the exterior-transport and dispersion modeling required by the SSRA. It is noted that SCIPUFF is accepted as one of EPA's alternative models for non-steady-state dispersion. However, the committee is concerned that the proprietary restrictions on the Joint

Effects Model (JEM) platform and the associated SCIPUFF version 2.4 component will limit the transparency of the risk assessment. Without sufficient transparency, the committee found it difficult to independently review and validate whether the proposed models would be appropriate for the SSRA. The CALPUFF Modeling System is the Environmental Protection Agency's (EPA's) standard for non-steady-state plume dispersal. While CALPUFF uses an older approach to plume modeling, it has the advantage of being an open platform with widespread use. Other models that were not considered in the work plan but are generally accepted by those modeling FMDv aerosol transmission are also worth investigating (Mikkelsen et al., 2003; Gloster et al., 2005a,b, 2010; Schley et al., 2009).

Selecting the right model for the SSRA is sufficiently complicated that the committee recommends DHS defer to the expert knowledge of its contractors for its final choice of method to simulate FMDv release plumes, with two caveats: (1) that their methods should conform to standard practice, and (2) that the methods be sufficiently open so interested parties can reasonably replicate their analysis and results. Therefore the platform chosen for the plume modeling should be an open platform to allow for independent review of the results of the risk assessment.

The committee did not ascertain whether modeling results would be used only for aerosol inhalation estimates or whether they would also feed into surface contamination estimates. The work plan will need to consider other exterior transport and dispersion modes, such as a scenario that includes pathogen transmission via truck tires.

Question 2.8. "Bulk" urban effects modeling: Due to the low urban density characteristics of the Manhattan area, do you agree with our proposal to model the "bulk" urban effects on the winds and turbulence?

Response to 2.8: The committee agrees that it is necessary for the SSRA to examine how local meteorology might enhance risk. The SSRA will have to particularly consider tornado climatology, since Kansas is tornado-prone. Topography is not likely to be a concern in Manhattan, Kansas, though its relatively flat terrain should still be considered in the assessment. With regard to the surrounding terrain, the atmospheric boundary layer, wind speed, and turbulence will vary with height depending on surface roughness[4]. Technology has not yet developed where it can take into account individual buildings and trees that can make the surface of the earth seem rough—where roughness of the ground creates wind speed profiles for speed and turbulence—and it may not need to because the effects of individual buildings would not be particularly important for the boundary layer. Sensitivity analyses will be needed to specifically address "bulk" effects (presumably referring to large-scale mixing and transport phenomena), and the committee expects that aerosol dispersal models will incorporate a sensitivity analysis for a reasonable range of atmospheric mixing patterns. A suburban profile is probably better to use than an urban profile that includes large, tall buildings and the effect of their turbulence wake. The committee reiterates that plume modeling should not be central to the SSRA.

[4] In engineering, terrain roughness is generally described as smooth (over water), fairly smooth (unobstructed by trees and buildings, such as an airport), rough suburban (with buildings and tress prevalent in suburban terrain), and urban with tall buildings (at the city center).

Prospective Epidemiological Study

Question 3.1. Parameters for FMDv release from NBAF: Does the NAS find the proposed parameters and assumptions acceptable? If not, what additional scientific evidence should be used to parameterize these qualities of FMDv?

Response to 3.1: The work plan attempts to calculate precise values by using imprecise parameters, unknown and unavailable data, and an imprecise model; given the paucity of data in the United States, the questions posed by the SSRA cannot be fully addressed using the available models. The results of the calculations will undoubtedly lead to a high probability of error and consequently impart false confidence in their reliability. A more measured approach using analogies from past experiences documented in the literature may be needed to balance the modeling approach which may be overly sensitive to underlying assumptions made in the model. The North American Animal Disease Spread Model (NAADSM) and other models allow users to control the mechanisms of transmission and infection dose, but are particularly sensitive to expert opinion for the underlying assumptions and thus are vulnerable to the foibles of expert opinion.

An ID_1[5] of FMD would be catastrophic to cattle; so the use of ID_{50}[6] rests on a flawed assumption. There is a need to include sensitivity analysis, and the committee recommends literature for more recent parameter estimates that have been published for dispersion models (Gloster et al., 2004, 2007, 2008, 2010; Sellers and Gloster, 2007; Schley et al., 2009).

Subpoint 1: The source article referenced (Alexandersen et al., 2003b) is a review; it is not primary literature, and it does not include original or observational data. The work plan will therefore need to be revised to use original or more recent data to determine the probability of infection. A possible solution would be to discuss these data values with Pirbright scholars during the SSRA team's planned visit to the Pirbright facility. The draft final SSRA report should include a table that lists the source of the data and the following categories: the number

[5] The term "ID_1" is an abbreviation for "Infectious Dose 1%," which is the amount that can be expected to cause infection in 1% of a group.

[6] The term "ID_{50}" is an abbreviation for "Infectious Dose 50%" or "Median Infectious Dose." The ID_{50} for a particular specimen of a pathogen is the amount that can be expected to cause infection in half (i.e. 50%) of a group of some particular animal species (of defined breed, genetic background, age, sex, weight, etc.), when inoculated or instilled by a particular route. In titrating an infectious agent, a series of dilutions of the test infectious material is made, and each dilution is inoculated into a set of replicate cell cultures or a small group of animals (for example, six to eight animals are often used at each dilution, spanning the expected end point). The cell cultures or animals are then observed or tested for evidence of infection and the results scored for a dilution endpoint determination. Reed and Muench (1938) and Kärber (1931) devised simple methods for estimating 50 percent dilution end points based on the total number of cell cultures or animals used in the titration, which gives the effect of using, at the two critical dilutions between which the endpoint lies, larger groups of cell cultures or animals than were actually used. These methods tend to define the dilution endpoint more narrowly than would be possible if it were simply determined by interpolation. Both the Reed-Muench and the Kärber methods are applicable primarily to complete titration series, that is, the whole reaction range, from 0 percent to 100 percent infectivity (or mortality or cytopathic effect, etc.). However, the methods have been utilized even when these conditions are not fulfilled, in some cases inappropriately. When the endpoint is *mortality* (of experimental animals), it is expressed as LD_{50} (50 percent lethal dose). ID_{50} indicates the dose which *infects* 50 percent of the test animals; $TCID_{50}$ indicates the dose which infects (or gives rise to cytopathic changes) in 50 percent of inoculated tissue culture tubes/chambers/wells/etc.

and age of animals exposed, the method of exposure, the method of verifying the dose delivered, the strain of FMDv used, the comparative virulence of that strain and other known strains, the length of time from exposure to a declaration of infected or not infected, how infection was verified, and confidence intervals on the dose-response modeling. The committee recommends that the SSRA examine the work of Haas and colleagues (1999) because it covers many of those issues in a quantitative microbial risk assessment.

Subpoint 2: The committee does not know what the infectious dose (ID) values are for wildlife, such as deer and feral swine, and believes that this information is unknown for the Manhattan, Kansas vicinity. A logical range of values that could be used would be based on published data on sheep and goats—probably the closest to wild ruminants—and on studies of FMD in domestic and feral swine. The effect of wildlife reservoirs on livestock infectivity is not known, but the possibility of establishing an endemic level of infection in wildlife that could pose a continuing threat should be considered. It will be important for the spread models to include wildlife, feral swine, and other non-domesticated susceptible species (such as those in zoos, game parks, and wildlife refuges) to ensure that the overall assessment is adequately comprehensive in addressing reasonable risks of infection and spread of FMDv.

Subpoint 3: It is unacceptable to ignore subclinical cases in swine or any other species, inasmuch as subclinical infections are critical in estimating the risk of transmitting diseases to other animals. Subclinically infected pigs could be especially dangerous because they may shed virus (Alexandersen et al., 2001, 2002; Alexandersen and Donaldson, 2002) and may be moved before an infection is detected. When exposed to low doses of FMDv, pigs can develop subclinical or mild forms of disease (Kitching and Alexandersen, 2002). On a herd basis, it is likely that some of those animals would eventually develop clinical disease and shed large quantities of virus.

Subpoint 4: A critical review of the biological factors associated with model inputs should accompany the choice of the aerosol dispersion model, as the committee was concerned about the proposed data inputs. The inactivation rates of airborne microbes vary significantly in response to environmental exposure. Some critical biological factors are not available as inputs, and those that were proposed were derived from literature and assumptions that are not appropriate or reliable as inputs for viral bioaerosols in the atmospheric environment. This includes, but is not limited to, environmental stability and infectivity decay rates of any of the viruses under consideration derived from limited and dates studies, as mentioned by the DHS contractor.

With the conglomerate of environmental affects on airborne microbial inactivation (such as humidity, temperature, and irradiance), the bioaerosol literature cited in the SSRA work plan is tenuous (Barlow, 1972; Donaldson, 1972; Donaldson and Ferris, 1975; Donaldson et al., 1983; Nuanualsuwan et al., 2008). Those studies cannot be reliably extended to provide model virus inputs because they are derived from aqueous environments, were surface associated (such as spider webs), or included anecdotal or incomplete information with specific regard to aerosol behavior. Modern bioaerosol studies—such as work from Tseng and Li (2005)—use carefully controlled chambers and molecular techniques to observe virus aerosol stability under a range of environmental conditions, and would be more appropriate for model inputs; however, FMDv and RVFV have yet to be stringently assessed using this emerging scientific paradigm, and only the most conservative of inactivation parameters may be assumed adequate for engineering-scale modeling.

Question 3.2. Extra-regional spread of FMD: Is our approach to mitigate the inability of NAADSM to model extra-regional spread acceptable? If not, is there an alternative approach to modeling extra-regional spread that addresses this shortfall?

Response to 3.2: Other models are capable of modeling spread in the United States (Bates et al., 2003a,b; Schoenbaum and Disney, 2003; Garner et al., 2007; Harvey et al., 2007); some have been the subjects of studies that compared predicted outcomes of models (Dube et al., 2007; Tildesley and Keeling, 2008). The NAADSM (Schoenbaum and Disney, 2003; Harvey et al., 2007) has been adopted by USDA's Center for Epidemiology and Animal Health because of its user-friendly interface, even though it has not been validated and may not be the best model for assessing spread and mitigation strategies. One study compared model spread predictions (Dube et al., 2007) and provided an estimate of how closely the predictions are correlated; it did not provide a validation of any model, and the SSRA work plan should not presume that the NAADSM has been validated by any reports in literature. The hypothetical spread of FMDv obtained by using NAADSM was compared with that based on AusSpread and Interspread models with a scenario that required simplified assumptions (Dube et al., 2007). Results indicated that the NAADSM yielded far fewer cases of FMD than the other two models.

The NAADSM and other models for consideration each have constraints that are subject to user bias and assumptions. The use of NAASDM, or any other model that might be used for the SSRA, should be supplemented with analysis of recent outbreaks to provide ground-truth data, in particular the effects of direct contacts (animal-to-animal) and indirect contacts (fomites, vectors, and personnel), delays in diagnosis, and the effectiveness of mitigation strategies in controlling disease spread.

The NAADSM would also need to model multi-regional outbreaks, given the extensive movement of cattle throughout Kansas and neighboring states that could contribute to rapid spread of infection during the time between the occurrence of a release and its detection. The number of cattle should be based on actual movement data, and such interstate movement data should be available from the Kansas state veterinarian's office. For dealing with spread of an infectious agent beyond the region of Manhattan, the risk assessment might consider network-based models similar to that used by Khan and colleagues (2009) to study H1N1 dispersal. That may provide a simpler and more direct assessment of interstate spread than the proposed approach based on the NAADSM alone. Specifically for FMD, the recent models of Keeling and colleagues (2001) and Tildesley and colleagues (2010) are particularly relevant to issues of regional spread and should be considered.

Question 3.3 Shortcomings of NAADSM: Are there additional shortcomings of NAADSM not presented here that we must mitigate to establish a robust system for predicting the spread of FMD from the NBAF?

Response to 3.3: As mentioned above, there might be limitations on available data; hence the NAADSM may yield a crude and potentially inaccurate assessment for the SSRA. The other models, such as the models of Keeling and colleagues (2001) and Tildesley and colleagues (2010), also would have difficulty with the poor quality or absence of data. In the absence of established or actual animal movement and contact data, the model can only assume or estimate uncorrelated (random) contacts; this may very well underestimate FMDv spread in that local networks of animal movement can accelerate spread compared with random contacts (direct or indirect) among premises. The constraints of whichever model used for the SSRA will need to be explicitly discussed.

In preparing this SSRA, there will be substantial uncertainty related to most components, including the laboratory's layout, pathogen characteristics, climate, ecology, environment, and economics. In communicating risk, the SSRA should not hide uncertainty with the complexity of quantitative models. When a modeling exercise is completed, the conclusions reached should only be valued to the extent that they improve mitigation measures and emergency response practices. Among explanations that have similar magnitudes of uncertainty, communication should rely on the simplest and most parsimonious mechanisms.

At the same time, the risk assessment should be able to respond to foreseeable changes in uncertainty, and the SSRA should consider mitigation plans for uncertain events. The SSRA will need to consider the potential consequences of events for which the risk is known with limited confidence, and develop plans for mitigating them. For example, estimates for the likelihood of a fomite-mediated pathogen release should be supplemented with consideration of the relevant mitigation models for that particular event. A comprehensive risk assessment will need to consider the mitigation contexts of risk estimates.

The committee is concerned that the proposed plan of work does not lay out a detailed plan of mitigation measure modeling. Mitigations measures are themselves complex. They are shaped by logistical and scientific constraints, and their efficacy can critically depend on the details of their implementation. For instance, detection of a release may be difficult for perhaps several weeks after its occurrence, depending on surveillance practices and the biology of the pathogen. That would have an important effect on the nature of mitigation measures after detection.

The design of mitigation measures for the NBAF will need to be an iterative process, with the risk assessment informing best practices and best practices informing the risk assessment. A more complete preliminary evaluation of mitigation practices is possible, perhaps on the basis of other laboratories' practices and response plans.

Question 3.4. Modeling of the contribution of wildlife: Is the proposed approach to assess the contribution of wildlife acceptable? If not, what changes are suggested to adequately consider the contribution of wildlife to an FMD outbreak to measure the utility of outbreak mitigation efforts?

Response to 3.4: So few data are available that it may be impossible to be conclusive about wildlife density, but the issue should certainly be mentioned. Some species of wildlife, including deer and feral swine, are susceptible to infection with FMDv (Kitching and Alexandersen, 2002), and in past outbreaks they have been destroyed because they pose a threat of infection to outdoor cattle and livestock (Ekboir, 1999).

In the event of a pathogen release from the laboratory, the ecology of the environment around the laboratory and the surrounding states may affect pathogen transmission and spread. However, few ecosystems are well understood. The compatibility of native host and vector species with an introduced pathogen is often unknown. Even when hosts are known to be compatible, research has shown that details of ecosystem structure, such as seasonal effects on the timing of pathogen life cycles, can control the presence or absence of endemic disease.

The local ecology is likely to be an important source of uncertainty unless there has been targeted research on the pathogen and host and vector species of concern. Rather than attempting to resolve such uncertainty without data, the risk assessment should document the potential for interactions with the local ecosystems and present facts about the demography of the species of concern.

Question 3.5. Approach to predict the spread of FMD from cases caused by a notional aerosol release: Overall, does NAS approve of the proposed approach to assess the effectiveness of site-specific risk mitigation strategies? If not, what are the NAS recommendations for improvement?

Response to 3.5: Risk-mitigation strategies are critical in a risk analysis but are underemphasized and lack detail in the work plan. The modeling of outbreak-mitigation strategies requires substantial attention and involves a variety of physical, biological, and economic constraints. A risk assessment should take into account the optimization of mitigation under such constraints and should bound outcomes within the practically and reasonably available mitigation practices. Capabilities, training, and equipping of emergency management, law enforcement, other emergency response organizations, and area hospitals and public health organizations should also be considered as a component of mitigation planning and strategy.

Economic Study

Question 4.1. Sufficiency of modeling beef and pork industries: Will restricting the economic effects to the beef and pork industries be satisfactory for this SSRA?

Response to 4.1: Restricting the analysis to the beef and pork sectors raises concern and leaves the analysis unnecessarily vulnerable to criticism. There will be spillover effects on other sectors—such as dairy, lamb and sheep, and feed crops, particularly forages—because of the animal population in the area of the facility. There will be effects on poultry and eggs with sympathetic price movements and changes in feed costs. Analysis of an outbreak that started in garbage feeding on a small, Midwestern swine operation shows that although the largest losses are confined to beef cattle and swine, the lamb and sheep sectors and poultry meat also experienced losses (Paarlberg et al., 2008). In the scenario analyzed, the dairy, egg, and crop sectors gain increased returns on capital and management (Paarlberg et al., 2008). There are options available to include other sectors. The SSRA could use the beef and pork model developed by Pendell and colleagues (2007) or by Zhao and colleagues (2006) and supplement it with models for dairy, poultry, feed grains, and wheat by using the models reported by Paarlberg and colleagues (2008). The advantage of the Pendell et al. model is that Kansas is identified separately from the rest of the United States, whereas the other models are national and have no regional flavor.

The design and methods presented lack depth and breadth of critical considerations for likely economic impacts, including loss of business, loss of government (including military) continuity and function, and economic losses to allied industries after placement of restrictions on the use of animal products for cosmetics and biologics development (for example, the inability to obtain fetal calf serum needed for tissue culture, vaccine development and production, pet foods, and the nutritional-supplement industry that uses “gel caps”). Analysis will need to address the costs associated with military intervention and involvement, assuming the Posse Comitatus Act or some other military action will be necessary, as was the case in the 2001 FMD outbreak in the UK (Chrisafis, 2001). The SSRA should also consider what military resources will be necessary and what it will cost to pull military personnel away from other operations to address an FMD epidemic in the United States.

Question 4.2. Interpretation of the term “region”: For both beef and pork, farm-level impacts are segregated between the affected U.S. region and the non-affected U.S. regions (rest of U.S.)

as well as impacts on beef and pork importers and exporters. Output from the epidemiological model will define the affected region and thus the number of animals affected. The SSRA team's interpretation of the term "region" is the area determined by the output of the epidemiological model (e.g., State of Kansas, specific counties). Does the NAS Committee agree with this interpretation? If not, please provide a recommended definition.

Response to 4.2: The committee disagrees with the interpretation of the term "region" in the SSRA; the region should be expanded to include neighboring states and the SSRA be expanded to include a national assessment as well because the economic impact of FMD will reverberate across state lines and nationally. The modeling should differentiate between regions within which animal movements are restricted and depopulation occurs and areas outside such regions. When one case of FMD is identified, all states will begin implementing plans to mitigate movement into and within their state. Thus, all states will be affected, and all will immediately begin to experience economic losses—closing of borders to milk or animal movement, stop-movement bans on livestock within states, and so on—even if a case has yet to be diagnosed in those states. The affected region will extend beyond the actual area of infection predicted by the models. A control zone with a radius of at least 10 km (6.2 miles)—covering a minimum of 120 square miles—will be established around each infected premises (Jon Zack, USDA-APHIS-VS, personal communication, January 26, 2010). All animal movement will be stopped in the control zone. Any dangerous-contact premises in the zone will probably be depopulated without waiting for evidence of infection. The definition of *region* should conform to anticipated control zones in the USDA–APHIS outlined FMD Preparedness and Response Plan (FMD PReP) (provided on request by the USDA–APHIS–VS National Center for Animal Health Emergency Management), including regions around secondary and tertiary spread.

National models—such as those of Devadoss et al. (2006), Zhao et al. (2006), Pendell et al. (2007), and Paarlberg et al. (2008)—generate price, quantity, and economic welfare changes from three potential shocks. One shock is the depopulation of animals relative to the national herd; the second is the loss of exports, as discussed below; and the third is potential adverse consumer reaction (Paarlberg et al., 2002). The aggregate of the three shocks determines national impacts. National impacts will reflect price changes but will not include government costs of maintaining containment regions or business costs of disruption in affected areas.

Question 4.3. Aggregation of output scenarios: Given the sizeable number of scenarios that may be generated by the plume and epidemiological models, will it be sufficient to aggregate the financial output values into high, medium and low economic impact categories? Each range provided will have specific dollar values indicated and specify the scenarios that are represented.

Response to 4.3: The scenarios can be aggregated. A critical driver of how the results can be grouped will probably be the duration of the outbreak. Because the losses from export restrictions and adverse consumer reactions are time-dependent (Paarlberg et al., 2008), outbreak duration is critical in the magnitude of effects (Paarlberg et al., 2009). The magnitude of animal depopulation also plays a role in determining which scenarios can be aggregated (Paarlberg et al., 2008). It is not possible to determine aggregation rules a priori, but it should be possible to aggregate once durations and supply losses are known.

Question 4.4. Trade ban timeframe: Economic studies specifically evaluating the impact of a domestic FMD outbreak differ in their assumptions of the length of the anticipated trade ban. Additionally, any projected length of trade ban is related to the duration and scope of the

impacted area. Trade ban is referring to the length of time the United States would not be permitted to trade because of an event (FMD outbreak). Based on a letter to DHS from the Director General, OIE (November 24, 2008) that states: "Once they could demonstrate that all cases could be contained within such zone and that no further cases were detected within a 30 day period, the entire country regained its FMD free status, within the only exception of the containment zone" we recommend a baseline trade ban of 45-60 days. Does the NAS Panel agree with this trade ban timeframe?

Response to 4.4: The trade ban length of 45–60 days is too short. The OIE director general's comment assumes that the United States could regionalize as Brazil and Argentina have during recent FMD outbreaks. However, the regionalization decision for the United States would need to be acceptable to importers, who would need to believe that the United States could isolate any FMD risk within the containment region. As in the situation of a potential outbreak of highly pathogenic avian influenza, it is the trade partners' response that determines whether regionalization occurs (Paarlberg et al., 2007). The key issues are the number of susceptible animals in the region relative to the U.S. herd and the extent of connections between the containment region and the rest of the livestock economy.

The question can be addressed by examining the animal population around Manhattan, using an assumed radius of 100 miles and an assumed radius of 200 miles to set an area that can be used to illustrate animal density. The area in question is primarily a beef-cattle region with some dairy cattle and swine, so the January 2009 total cattle inventory data by county can be used (USDA-NASS, 2009).

A 100-mile radius extends eastward to Kansas City; northward to include Beatrice, Nebraska; southward to south central Kansas; and westward nearly to Russell, Kansas. The area contains about 2% of the total U.S. cattle inventory (USDA-NASS, 2009).

Extending the radius to 200 miles means a north–south range from about Norfolk, Nebraska, to Tulsa, Oklahoma. The east–west range is from just beyond Sedalia, Missouri, almost to Oakley, Kansas. The area examined includes most of Kansas, large parts of Nebraska and Missouri, western Iowa, and northern Oklahoma. Including western Iowa and Missouri means that substantial regions of swine production fall within the circle. Roughly 9.5% of the U.S. cattle inventory is in this area (USDA-NASS, 2009).

With respect to transportation, the circle within a 100-mile radius includes long sections of Interstates 70 and 135. It includes westward rail service out of Kansas City. Extending the zone to a 200-mile radius adds sections of Interstates 80 and 29 and the main line of the Union Pacific Railroad. Kansas City, Hastings, and Grand Island, Nebraska, are well within the larger zone. The cities included have several meatpacking plants. Omaha, Nebraska, and its stockyards are in the larger circle. Norfolk, Nebraska; Tulsa, Oklahoma; and Council Bluffs and Sioux City, Iowa, are in the zone or on its perimeter.

The ability to isolate the region seems unlikely, given the share of the U.S. cattle inventory in the circles, the transportation links across them, the Omaha stockyards, and the packing plants in the cities included. Thus, trade partners probably would not accept regionalization. Japan and Korea have been major trading partners for meat. They did not regionalize after the cases of bovine spongiform encephalopathy (BSE) in the United States and Canada, nor did they regionalize after the FMD outbreaks in Taiwan and Britain. Therefore, it is assumed that the United States could not regionalize an outbreak centered in Manhattan, Kansas.

For a country like the United States, which is initially FMD-free and does not vaccinate, the time to regain FMD-free status will depend on the control actions taken during an outbreak.

If there is a stamping-out policy (that is, depopulation) and serological surveillance without emergency vaccination, FMD-free status could be regained as soon as 3 months after the last case (OIE, 2009). If emergency vaccination is undertaken in conjunction with a stamping-out policy and serological surveillance, FMD-free status could be regained 3 months after the last vaccinated animal is slaughtered (OIE, 2009). If vaccinated animals are not slaughtered, the time to recover FMD-free status changes to 6 months after the last case and is contingent on the results of a serological survey (OIE, 2009).

The OIE Terrestrial Animal Health Code, in Articles 8.5.10–8.5.31, identifies importation guidelines for animals and animal products. For animals, recommendations are for international veterinary certificates that indicate that the animals have no signs of FMD and were isolated and quarantined for 30 days to 3 months before export, depending on the exporting nation's disease status with negative FMD diagnostic tests (OIE, 2009). Similar rules apply to semen and embryos from donor animals included in isolation, quarantine, and tests (OIE, 2009).

Meat can be imported from countries with cases of FMD with the following recommendations: the entire shipment comes from an approved slaughterhouse that has ante-mortem and post-mortem inspections for FMD, and the meat has been processed to destroy FMDv. OIE Article 8.5.32 describes such processing as consisting of canning of meat heated to 70°C for 30 minutes, cooking deboned and defatted meat up to an internal temperature of 70°C for 30 minutes, or drying salted, deboned meat. Imported milk, cream, and milk product also are to have a veterinary certificate stating that they originated in FMD-free herds and have been processed to destroy the virus (OIE, 2009). Such processing includes heat treatments and hermetic sealing in containers. Cheese, butter, and yogurt are generally not restricted, but condensed milk, sterilized milk, and casein may be restricted (OIE, 2009). FMDv transmission from animals to humans is rare and is not a public health concern.

Evidence from other exporters with FMD suggests delay in export recovery beyond the OIE guidelines. Taiwan experienced an outbreak in spring 1997 (USDA-FAS, 1997). Before the outbreak, that nation exported pork to Japan. As a consequence of the outbreak, exports were stopped, and they have not recovered as Taiwan regionalized its pork industry (USDA-FAS, 1998, 2000).

Britain experienced an FMD outbreak starting at the end of February 2001, with the last cases occurring the week of September 24 (UK-MAFF, 2002). An important dimension of the British situation is the presence of BSE and the fact that a link between BSE and variant Creutzfeldt-Jakob disease in humans had been announced in March 1996 (Brown, 1997). Export restrictions were imposed immediately by the British government (USDA-FAS, 2001). Restrictions imposed by the European Union on British exports were lifted a year later, on March 6, 2002 (Johnson, 2005). Japan lifted its restrictions on October 6, 2003 (Johnson, 2005). Despite the end of all restrictions on British exports, exports did not return to pre-outbreak levels until fall 2004 (Johnson, 2005). The quarterly pattern shows that British exports did not begin to recover until the second quarter of 2002, 3 quarters after the last reported case (Johnson, 2005). Exports recovered throughout 2002 and reached a plateau in the first half of 2003 (Johnson, 2005). Starting in late 2003, exports moved to a new plateau, which lasted until summer 2004; recovery was complete in fall 2004 (Johnson, 2005).

For FMD, the export impacts might be a total ban on exports of beef, pork, lamb, beef cattle, dairy cattle, hogs, lambs, and sheep during and 1 quarter after the outbreak. On the basis of the product rules set out by OIE and U.S. export data from the U.S. International Trade Commission, about one-third of dairy product exports could also be lost (USITC, 2009). Exports

would gradually recover, as did British exports, with full recovery perhaps 8 quarters after recovery begins. Trading partners have a strong economic motivation to delay accepting imports. The SSRA should consider the extensive losses to the swine industry due to the outbreak of pandemic H1N1 virus (so-called swine flu) as an instructive model. No pigs in the United States were detected as infected; however, major trading partners used the opportunity to reduce imports of U.S. pork. Any consideration of economic consequences will need to acknowledge the possibility of a similar reaction if it is to have credibility in the livestock industry.

Question 4.5. Critical economic infrastructure threshold: We propose the critical economic infrastructure include; the value of livestock affected directly or indirectly by an outbreak, and the value of any damage to facilities and equipment in the case of an accidental or intentional release. Does the NAS panel agree with this definition, if not, what modifications to this definition should be made?

Response to 4.5: The critical economic infrastructure should include

1. The prevailing market value before the epidemic of livestock depopulation;
2. The change in returns to livestock producers with animals not depopulated;
3. The changes in returns to upstream and downstream industries;
4. Changes in consumer welfare;
5. Effects on nonagricultural sectors; and
6. Effects on the local, state, and national communities—employment, and so on.

The first four should be determined by the agricultural sector model used to determine the national effects of the outbreak on agriculture. Effects on non-agricultural sectors could be determined from an applied general equilibrium model of the United States. Devadoss and colleagues (2006) used such a model to examine BSE, and DHS should be able to gain access to that model. Effects on the local community of Manhattan could be generated with regional input–output modeling.

Final Report

Question 5.1. **Content and order of Final Report outline:** Is the content and general order of items presented in the Final Report Draft Outline acceptable?

Response to 5.1: The general order of items presented in the final report draft outline is acceptable. However, the contents of the draft report should be revised to address the committee's general concerns regarding the SSRA's pathways, pathogens and hosts, practices, mitigation strategies, and site-specific analysis. The committee would like the SSRA to include a scenario for Nipah virus or Hendra virus escape, and for the acquisition and handling of a highly pathogenic emerging zoonotic agent with unknown characteristics (perhaps using the example of how Nipah, a previously unknown BSL-4 pathogen, was handled from a diagnostic sample).

Question 5.2. Final Report outline topics: Are there topics that should be added, deleted, or for which the order should be changed?

Response to 5.2: The committee proposes a few suggested changes in Appendix B-1.

Rift Valley Fever Amendment

Amendment Question 1: Parameters for RVFV release from NBAF: Do these parameters reflect the best available scientific evidence? If not, what evidence should be used to parameterize these qualities of RVFV? We will perform sensitivity analysis with each uncertain parameter to understand the effect of uncertainty on our analysis.

Response to Amendment Question 1: A justification was not provided for the selection of the SCIPUFF model over other dispersion models, and no peer-reviewed literature was provided. As indicated by the World Health Organization, aerosol is not the main transmission route of Rift Valley fever virus (RVFV) (WHO, 2007). The committee reiterates its concern about the SSRA's basing its epidemiological modeling exclusively on airborne escape from the laboratory. As mentioned above, the four routes recommended for FMDv would apply similarly to RVFV and all other pathogens that may be studied in the NBAF.

The SSRA should present the key primary data and source references. The committee recommends that the SSRA receive substantial input from subject matter experts to assist with literature reviews and to obtain parameter data. As noted above for FMDv, details on the ID-response determinations remain important for any other animal pathogens and zoonotic agents considered for study. The relevance of the test animals in the infectious dose studies, dosing, dosing determination, relative virulence of organism strains, and comparative response in humans (in the case of zoonotic pathogens) should be appropriately summarized with citations to source data. As in the case of FMDv dispersion, LD_{50} is inappropriate inasmuch as it is necessary for only one animal or person to be infected (LD_1) for an RVFV escape to have catastrophic consequences.

Before dismissing the wildlife component, the type and distribution of wildlife (beyond deer) that exist in the region should be determined.

Amendment Question 2: Evidence basis of prospective epidemiological RVF modeling: Is the evidence basis for the prospective epidemiological modeling of RVF within non-endemic areas sufficient to produce a useful and defensible model?

Response to Amendment Question 2: The evidence provided by the SSRA work plan is inadequate to support an epidemiological RVFV model for spread and dispersion. The epidemiological RVFV model will need to adequately differentiate urban and rural areas. Vector spread of RVFV and the theoretical risk of human-to-human transmission of the virus from infected patients to healthcare workers in Manhattan, Kansas, would probably be quite different from those in rural areas of the developing world on which there are data. In its epidemiological model and mitigation strategy, the SSRA should also include the likelihood of eradicating and the time needed to eradicate infected vectors and infected animal reservoirs, such as cattle and sheep.

Amendment Question 3: Robustness of prospective epidemiological RVF modeling: Overall, is this approach robust and evidence-based enough to adequately assess the effectiveness of risk mitigation strategies in this project? If this approach is not considered robust enough for this project, how should this approach be improved?

Response to Amendment Question 3: RVF is a vector-borne disease, so the SSRA will especially need to consider the possibility of a laboratory worker being bitten by an RVFV-

infected mosquito or the possibility of RVFV-infected mosquitoes' escaping from containment. The SSRA will also need to address mitigation steps for a zoonotic disease that can be maintained in animal hosts and mosquitoes and their eggs. One crucial mitigation step would be a public education campaign about RVF so that members of the public will know how to protect themselves and how to recognize signs of disease in humans and animals. Ruminants are amplifying hosts, so an important mitigation strategy would be to have a stockpile of RVF vaccine available for use in ruminants in the event of an outbreak by the time the NBAF opens. Other elements of mitigation to be considered should include vector control, spraying, testing, and surveillance implementation to test for RVFV in potential host populations, including humans.

Amendment Question 4: Parametric approach to cost of illness: Data which establish the cost of illness (COI) resulting from the introduction of RVF will be estimated parametrically from related economic impact studies of other zoonotic diseases (e.g., West Nile Virus, H5N1, H1N1). Does the NAS Committee concur with this approach and are there any specific references/studies suggested that may assist the team with this aspect of the analysis?

Response to Amendment Question 4: The parametric approach to the cost of illness proposed by the SSRA does not take into account the science and biology of RVF, but it will need to do so. The economic impact studies from H1N1 and H5N1 will not necessarily apply to a vector-borne zoonosis such as RVF, thus the model is not a one-size-fits-all model. The cost of an illness will depend on its severity and treatment for it, so the cost incurred because of RVF should be different from the cost incurred because of H1N1 or H5N1 influenza or West Nile virus (WNV), and the difference will have to be incorporated into the economic assessment. Also, assessing the cost of illness for RVF is complex because the assessment will need to consider impacts on both human and animal populations.

Estimates for major economic losses due to livestock and trade restrictions for RVF-infected livestock can be quantifiable. Determination of the cost of infection should consider costs associated with animal morbidity, including abortion. An outbreak of RVF would cause U.S. trading partners to stop importation of at least beef and lamb, and perhaps pork, until there is proof that RVFV has been eliminated. It will be difficult to conduct surveillance to prove that the nation is free of RVFV, given that the virus is capable of surviving in mosquito eggs for extended periods of time (WHO, 2007).

However, to address the cost of illness for humans alone, the assessment would need to include the cost of disease, public health response costs, direct healthcare costs, productivity losses, and additional economic costs. As an example, the economic impact from the 329 cases in the 2002 Louisiana WNV epidemic resulted in $20.1 million in human medical, non-medical, and public health response costs (Zohrabian et al., 2004). However, for a pathogen such as RVFV, there is no evidence of RVF outbreaks in urban areas (WHO, 2007) and the likelihood of North American mosquitoes acting as efficient RVFV vectors outside the laboratory setting is still uncertain (Turell et al., 2008). Furthermore, it is uncertain how the economic impacts on human health for RVF in developing countries would translate to potential economic health impacts in the United States where the healthcare system differs. Thus the committee believes it would be difficult to provide a reliable estimate for the cost of illness for RVF by benchmarking it to other zoonoses.

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Appendix B-1

Committee's Revisions to Draft Final Report Outline

The committee's suggested revisions to the draft final report outline are noted in bolded underline for additions and strikethrough for deletions.

I. Executive Summary
   a. Overview
      i. NBAF Purpose and Benefits
      ii. Site-Specific Risk Assessment Objectives
   b. Results
      i. Best Practices Overview for Manhattan Design and Operations
         1. Design
         2. Operations
         3. Mitigation
      ii. Reasonable **Maximum Credible Risk** ~~Worst-Case~~ Scenario Outcomes
         1. Assumptions
            a. Baseline Best Practices
            b. Site-Specific Considerations
         2. Outcomes and Impact
            a. Extent of Pathogen Dispersion
            b. Potential Spread of Associated Disease
            c. Economic Impact
   c. Site-Specific Risk Assessment Conclusions and Recommendations
II. Purpose and Objectives
   a. Define Best Practices
      i. Design and Construction
      ii. Operations
      iii. Personnel reliability (consider this to be handled by DHS and not specific to the SSRA)
      iv. Emergency and Contingency Planning
   b. Identify Potential Release Scenarios
      i. Accidental
      ii. Intentional
   c. Model Outcomes
      i. Fate and Transport ~~Plume~~ Modeling **(through 4 categories of pathways)**
         1. air
         2. solid waste

3. **liquid waste**
4. **in/on fomites or hosts**

ii. Epidemiological Modeling
iii. Economic Consequence Assessments

d. Develop Strategies for Prevention and Mitigation of Reasonable **Maximum Credible Risk** ~~Worst-Case~~ Scenarios

III. Technical Approach

a. Expertise
   i. Subject Matter Experts
   ii. Key Personnel
b. Risk Management
c. Technical Tasks
   i. Emergency and Contingency Planning Requirements Review and Baseline Mitigation Strategy Development (Task 01)
      1. Review of Best Practices, **Mitigation Strategies, Risk Communication,** and Emergency Response Plans at Domestic and International Sites
      2. Review of Findings with US Government Team and Discussion of NBAF Response Plans **with national, regional, state, and local responders**
      3. Development of a Baseline Mitigation Strategy for the NBAF including Local/State/Federal strategies.
   ii. Scenario Review (Task 02)
      1. Scenario Database Development and Boundary Conditions
      2. SME Panel Scenario Review
   iii. Data Collection (Task 08)
      1. Animal
      2. Transportation
      3. Human Population and Health
      4. Insect Vector
      5. Building
   iv. ~~Plume~~ Modeling (Task 04)
      1. Model and Source Term Development
      2. Meteorological Data Preparation
      3. Modeling Plan Development and Review
      4. Model Setup
      5. Modeling Simulations
      6. Post-process Model Results Evaluation
      7. ~~Plume~~ Model Report Development and Review
   v. Epidemiological Study (Task 05)
      1. Data Collection
      2. Existing Epidemiological Model Assessment
      3. FMDv **and RVFV** Model Development
      4. Parametric Assessment of FMDv **and RVFV** Release
   vi. Economic Study (Task 06)
      1. Pre-release Market Conditions Assessment
      2. Post-release Market Conditions Assessment
      3. Animal Commodity Flow

4. Containment and Animal Stop Zones
5. Critical Economic Infrastructure and Key Resources
6. Trade Impacts
7. Economic Study Report Development and Review

d. Process and Data Flow
e. Reports and Deliverables (Task 07, plus portions of Tasks 2,4,5,6,& 8)

IV. Results
a. Best Practices
b. Data Collection
c. Scenario Database
d. ~~Plume~~ Modeling
e. Epidemiological Studies
f. Economic Studies
g. Risks

V. Conclusions and Recommendations
a. Reasonable **Maximum Credible Risk** ~~Worst-Case~~ Scenario Outcomes
b. Reasonable **Maximum Credible Risk** ~~Worst-Case~~ Scenario Mitigation Strategy
c. Recommendations

VI. Bibliography

VII. Supporting Data (*Order subject to change dependant on order in which they are referenced in the Final Report*)
a. Appendix A: Collected Data Sets
b. Appendix B: Best Practices: Response Strategies
c. Appendix C: Best Practices: Mitigation Strategies
d. Appendix D: Scenario Database
e. Appendix E: ~~Plume~~ Models (*Modeling Plans and Final Report*)
f. Appendix F: Epidemiological Models
g. Appendix G: Economic Consequence Models

Appendix C

Public Meeting Agendas

February 26, 2010
Washington, DC

8:30 – 8:40 a.m.	**Welcome and Introductions** *Ron Atlas, Chair*
8:40 – 9:00 a.m.	**Introduction to the National Bio- and Agro-Defense Facility (NBAF) Site-Specific Risk Assessment (SSRA)** *Jamie Johnson, Director, Office of National Laboratories, DHS*
9:00 – 9:45 a.m.	**Overview of the NBAF SSRA Work Plan** *Adam Hamilton, Signature Science*
9:45 – 10:15 a.m.	**Background and Overview of the Work Plan Questions** *Julie Brewer, NBAF Project Manager*
10:15 – 10:30 a.m.	Break
10:30 – 12:15 p.m.	**Discussion** *Moderator: Ron Atlas, Chair*
12:15 – 12:30 p.m.	**Concluding Remarks** *Ron Atlas, Chair*

July 13, 2010
Washington, DC

1:00 – 1:15 p.m.	**Welcome and Introductions** *Ron Atlas, Chair*
1:15 – 1:25	**Introductory Remarks by DHS** *Jamie Johnson, Director, Office of National Laboratories, DHS*
1:25 – 3:00	**Q&A Session with Committee** *Moderator: Ron Atlas, Chair*
3:00 – 3:15	Break
3:15 – 4:00	**Q&A Session with Committee (cont'd)** *Moderator: Ron Atlas, Chair*
4:00 – 4:15	**Public Comments** *Please register ahead of time*
4:15 – 4:30	**Concluding Remarks** *Ron Atlas, Chair*
4:30	**Adjourn open session**