#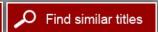 Evaluation of the Updated Site-Specific Risk Assessment for the National Bio- and Agro-Defense Facility in Manhattan, Kansas

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Evaluation of the Updated

Site-Specific Risk Assessment for the

NATIONAL BIO- AND AGRO-DEFENSE

FACILITY IN MANHATTAN, KANSAS

Committee on the Evaluation of the Updated Site-Specific Risk Assessment
for the National Bio- and Agro-Defense Facility in Manhattan, Kansas

Board on Life Sciences

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Acknowledgments

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:

Nancy D. Connell, *University of Medicine and Dentistry of New Jersey*
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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 **Dr. Lynn Goldman, George Washington University, and Dr. Ann Arvin, Stanford University School of Medicine**. 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.

Preface

Protecting the nation's food supply system from foreign animal diseases and protecting our citizenry and the peoples of the world from zoonotic diseases requires advanced research capabilities. That in turn means that there is a need for safe and highly secure laboratories in which to conduct research, develop diagnostic capabilities, and develop vaccines. To that end, the Department of Homeland Security (DHS) is planning to construct a new National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas, to replace the aging Plum Island Animal Disease Center in New York. Once completed, the NBAF will join facilities in Australia, Canada, and Germany to become the fourth functioning biosafety level 4 (BSL-4) agricultural research center in the world to conduct work on large animals.

Foreign animal diseases, such as foot-and-mouth disease (FMD), are ones that are not endemic in the United States and may have a great impact on our agricultural economy if an outbreak occurs in the United States. Many important foreign animal diseases are not zoonotic and cannot be transmitted to humans. Nonetheless, they pose a threat of immense economic impact on American agriculture. Other high-consequence biological threats involving animal and zoonotic diseases will also be studied at the NBAF. About 65% of emerging infectious diseases over the last 50 years have been zoonotic. Studying emerging and new infectious diseases will require capabilities for research with large animals (including BSL-4), and these capabilities will be critical for addressing future unknown threats.

Although there is wide agreement that the country needs a facility like the NBAF, the Government Accountability Office raised the question of whether FMD research can be safely conducted on the mainland of the

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United States. When the decision was made to construct the facility in Manhattan, Kansas, further concerns were raised about building the facility in the middle of Tornado Alley and in the heart of cattle country. Congress thus instructed DHS to conduct a site-specific risk assessment (SSRA) of the potential release of FMD virus from the new facility in Manhattan and the consequent infection, spread, and economic impact. Congress further instructed DHS to seek a review of the risk assessment by a scientific and technical committee of the National Research Council.

DHS and its contractors prepared the site-specific risk assessment and made it public in 2010, and it was reviewed by a committee of the National Research Council. While that committee found the assessment to be a notable first step in an iterative process aimed at identifying and minimizing risk and determining actions that will need to be taken, it nonetheless found the assessment not entirely adequate or valid. Congress subsequently mandated in the Department of Defense and Full-Year Continuing Appropriations Act of 2011 (P.L. 112-10, Sec. 1647) that DHS prepare an updated SSRA (uSSRA) to address concerns raised by the committee's review.

The uSSRA is based on the 65% design phase planning documents for the facility and the uSSRA is the subject of this committee's evaluation. The present report is directed to Congress, DHS, stakeholders among the nation's citizenry, and interested scientific and technical communities.

As noted in the 2009 National Research Council report *Science and Decisions*: "risk assessment has become a dominant public-policy tool for informing risk managers and the public about the different policy options for protecting public health and the environment. Risk assessment has been instrumental in fulfilling the missions of . . . federal and state agencies in evaluating public-health concerns, informing regulatory and technologic decisions, setting priorities for research and funding, and developing approaches for cost-benefit analyses." The purposes of risk assessment in the context of the NBAF are to

• Provide a systematic and valid approach to evaluating potential accident events and scenarios that might lead to the release of pathogens from the facility in Manhattan, Kansas, and the potential consequences thereof.

• Include surveillance, response, and mitigation plans for detecting and controlling the spread of disease.

• Characterize uncertainties in calculated results based on state-of-the-art risk analysis practice.

• Incorporate peer-reviewed and validated models and scientific data in the analysis.

• Develop and use a method of estimating the cumulative risk of an FMD infection resulting from an accidental release from the Kansas site over the operating lifetime of the facility.

In the process of reviewing the uSSRA, the committee had the opportunity to hear public comments on the proposed facility and on the risk assessment. These were heard during public sessions in Washington, DC, and during a visit to the proposed site in Manhattan, Kansas, and a tour of the existing Kansas State University Biosecurity Research Institute. The purpose of the site visit was for the committee to better understand specific considerations for the facility. The committee thanks the many members of the public who contributed comments to the evaluation process.

The committee also acknowledges and thanks the U.S. and international experts who volunteered their time to attend early meetings of the committee and to provide their perspectives and experience. They included Soren Alexandersen, Christopher Broder, Charles Haas, Michael Johnson, Thomas Ksiazek, Paul Langevin, Thomas Mettenleiter, Gay Miller, Gregory Paoli, Barrett Slenning, Gregory Smith, Alfonso Torres, Hana Weingartl, and Neal Woollen.

On behalf of the committee, I would like to thank the National Research Council staff who invested great effort and energy in supporting the committee's work throughout the preparation of this report. I also thank the members of the committee for unselfishly contributing their services and for the collegiality of their efforts.

Gregory B. Baecher, *Chair*
Committee on the Evaluation of the Updated
Site-Specific Risk Assessment for the
National Bio- and Agro-Defense Facility in Manhattan, Kansas

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BOXES

Acronyms and Abbreviations

ABSL	animal biosafety level
ACRE	average crop revenue election
AHR	animal handling room
ATR	transfer of aerosolized infectious material into the nasal passages of a researcher when researchers are in an AHR
BSL	biosafety level
CDC	Centers for Disease Control and Prevention
DHS	U.S. Department of Homeland Security
EIS	environmental impact statement
EMAP	Emergency Management Accreditation Program
FAD	foreign animal disease
FMD	foot-and-mouth disease
FMDv	foot-and-mouth disease virus
GAO	U.S. Government Accountability Office
HEPA	high-efficiency particulate air
HeV	Hendra virus
HRA	human reliability analysis
HSPD-9	Homeland Security Presidential Directive 9

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IATA	International Air Transport Association
IOM	Institute of Medicine
KDE	kernel density estimation
KDHE	Kansas Department of Health and Environment
LD	lethal dose
MAR	material available for release
NAADSM	North American Animal Disease Spread Model
NAHLN	National Animal Health Laboratory Network
NBAF	National Bio- and Agro-Defense Facility
NFPA	National Fire Protection Association
NiV	Nipah virus
NOAA	U.S. National Oceanic and Atmospheric Administration
OIE	World Organization for Animal Health
OTB	spill of a shipment of FMDv results in transference to the body in non-containment areas
PFU	plaque-forming unit
PIADC	Plum Island Animal Disease Center
PNNL	Pacific Northwest National Laboratory
POE	probability of exceedance
RIMS II	Regional Input-Output Modeling System
SCIPUFF	Second-order Closure Integrated Puff Model
SOP	standard operating procedure
SSRA	site-specific risk assessment
USAMRIID	U.S. Army Medical Research Institute for Infectious Diseases
USDA	U.S. Department of Agriculture
USGS	U.S. Geological Survey
uSSRA	updated site-specific risk assessment

Summary

Safeguarding U.S. agriculture from foreign animal diseases and protecting our food system require cutting-edge research and diagnostic capabilities. The Department of Homeland Security (DHS) and the U.S. Department of Agriculture (USDA) have embarked on an important mission to replace the aging Plum Island Animal Disease Center with a new facility, the National Bio- and Agro-Defense Facility (NBAF). When operational, this new facility would be the world's fourth biosafety level 4 laboratory capable of large animal research. It would serve as a critical world reference laboratory for identifying emerging and unknown disease threats, and would thus be a critical asset in securing the future health, wealth, and security of the nation.

DHS selected Manhattan, Kansas, as the site for the new NBAF after an extensive site-selection process that involved an environmental impact statement. The Government Accountability Office raised concerns about DHS's analysis of the potential spread of foot-and-mouth disease virus (FMDv), one of the most serious foreign animal disease threats. Congress subsequently directed DHS to conduct a site-specific risk assessment (SSRA) for the NBAF, instructed the National Research Council (NRC) to independently evaluate the SSRA, and prohibited obligation of NBAF construction funds until the NRC review was complete (P.L. 111-83).

The NRC review found that the 2010 SSRA was inadequate due to flawed methods and assumptions which potentially underestimated the risk of an accidental FMDv release from the NBAF in Manhattan, Kansas. In response, Congress mandated that DHS revise its SSRA to address shortcomings, directed the NRC to evaluate the updated SSRA (uSSRA), and

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again prohibited obligation of construction funds until the completion of the second review (P.L. 112-10). The scope for both the 2010 SSRA and the 2012 uSSRA addressed accidental release of pathogens from the NBAF in Manhattan, Kansas, and excluded terrorist acts and malicious threats from its risk assessments.

The NRC convened a committee of experts to evaluate the adequacy and validity of the uSSRA. This report is the committee's evaluation of the final uSSRA.

OVERALL ASSESSMENT

The committee evaluated the uSSRA provided by DHS in February 2012 and finds that it is a substantial improvement over the original 2010 SSRA. DHS and its contractors should be commended for this effort. Many of the shortcomings identified by the previous committee have been addressed in the uSSRA, and this has resulted in a more quantitative and transparent analysis. The uSSRA uses more conventional risk assessment methods and better complies with standard practice than did the 2010 SSRA. In general, the descriptions of the approaches are clear, and the uSSRA uses appropriate conceptual models and methods.

The quantitative conclusions of the uSSRA differ dramatically from those of the 2010 SSRA. Data and methods of the previous risk assessment led to a conclusion that for the two scenarios with the greatest risk of FMDv release (fomite and worker without respiratory protection), there would be a 70% probability that FMDv release would cause an infection resulting in an outbreak during the 50-year life span of the NBAF in Manhattan, Kansas. In contrast, the uSSRA concludes that the cumulative probability for 142 risk events (including catastrophic events such as tornadoes and earthquakes) leading to an accidental release of FMDv over 50 years is about 0.11% (or 1 in 46,000 per year), which is orders of magnitude lower than the first estimate. Improvements in the 65% design phase documents for the facility compared with the earlier and less complete design documents on which the 2010 SSRA was based may explain some of the risk reduction. However, the committee believes that questionable and inappropriate assumptions were used in the uSSRA that led to artificially lower estimates of the probabilities and amounts of pathogen released.

In contrast with the 2010 SSRA, which cited fomites and lack of respiratory protection as the most likely pathways of accidental FMDv release, the uSSRA concludes that the most likely release mechanisms are those associated with natural hazards, specifically earthquakes and tornadoes. The uSSRA concludes that these are about 20 times more likely than operational pathways.

Despite improvements, the committee finds that the uSSRA under-

estimates the risks of pathogen release and infection and inadequately characterizes the uncertainties in those risks. The committee finds that the extremely low probabilities of release are based on overly optimistic and unsupported estimates of human error rates, underestimates of infectious material available for release, and inappropriate treatment of dependencies, uncertainties, and sensitivities in calculating release probabilities.

The committee is concerned that the vanishingly small estimates of risk found throughout the uSSRA are inconsistent with most modern, complex industrial systems. In many instances, the committee could not verify uSSRA results, because methods and data were unevenly or poorly presented. The uSSRA also contains inconsistent information, which made it difficult to interpret data or to reconstruct risk scenarios, and thereby made it difficult to determine the degree to which risks were underestimated.

The committee recognizes that significant complexities accompany a risk assessment of this nature, yet the practice of risk analysis is sufficiently mature to be able to treat such complexities and therefore the committee's expectations for such a risk assessment are customary and attainable. The number of facilities comparable with the NBAF is small, so there is little empirical validation of the risk estimates. However, because a pathogen release from the NBAF could have devastating agricultural, economic, and public health consequences, a risk assessment that reaches inappropriate conclusions could have substantial repercussions.

The committee has identified a number of deficiencies that lead to the conclusion that the uSSRA continues to be inadequate in characterizing the risks associated with operating the NBAF in Manhattan, Kansas.

FINDINGS

Finding 1: The uSSRA addresses many, but not all, of the issues outlined in the congressional mandate. The uSSRA attempts a quantitative risk assessment and attempts to model FMDv release and infection from the proposed NBAF in Manhattan, Kansas. However, it does not adequately include overall risks associated with the most dangerous pathogens in its biosafety level 4 (BSL-4) assessment.

Finding 2: The 65% design phase plans for the facility appear to be sound. The NBAF design plans provided to the committee—which were at only 65% completion—appear to have been competently executed by architects and engineers experienced with modern biocontainment laboratories, and the designs appear to conform to international safety standards for similar facilities. Although DHS stated that those conducting the risk assessment consulted the building designs, the uSSRA does not seem to clearly reflect design changes or to incorporate design

provisions in the risk assessment (i.e., natural hazards assessments not reflecting 65% design plans that harden the structure against tornadoes). The committee recognizes that it is necessary and challenging to integrate design improvements to produce an informed risk assessment. It is important to note that inadequacies in the uSSRA do not necessarily imply inadequacies in the design of the facility itself. Any conclusions about the adequacy and validity of the uSSRA should not be construed to imply similar conclusions with respect to the quality of the 65% design plans.

Finding 3: The uSSRA misinterprets and misapplies some risk methods, which have implications for the entire risk assessment. The uSSRA adopts some risk assessment methods that are in line with current practice, including the application of event tree analysis and other methods of quantitative probabilistic risk assessment. The modeling framework used is a "scenario-based" approach that is a well-established approach to risk analysis of complex systems and processes. However, those risk assessment methods are inconsistently applied across the various sections of the report.

Finding 4: The uSSRA ignores probabilistic dependencies in calculating risk scenarios, and this results in potentially serious underestimations of total risk and incorrect ranking of risk contributors. Use of questionable or erroneous methods and assumptions about probabilistic dependencies in portions of the uSSRA most likely results in an underestimation of the probability of accidental FMDv release.

Finding 5: The characterization and assessment of uncertainties are incomplete and inconsistent, and this leads to a false sense of precision. Sensitivity analyses and a quantitative assessment of the uncertainties in key model assumptions, model parameters, and risk results are required for the uSSRA to be viewed as adequate. The lack of full assessment of uncertainties is a serious deficiency in the uSSRA and limits its utility for decision making.

Finding 6: The uSSRA applies very low human error rates and uses methods that omit important error pathways, which likely resulted in low estimated probabilities of release. Probabilities of human error used in the uSSRA appear not to be based on published literature or empirical experience. The 2010 SSRA concluded that human error would be the most likely cause of release, and the previous committee agreed with that conclusion (see Finding 9 of 2010 NRC report *Evaluation of a Site-Specific Risk Assessment for the Department of*

Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas). Little justification is provided for the uSSRA's optimistic assumption that the rate of human error for NBAF workers will be several times less than that of similarly skilled workers in similar facilities.

Finding 7: The uSSRA appears overly optimistic in its assignment of parameter values to models, yet describes those values as conservative. Underestimates of parameter values by one or two orders of magnitude—when taken together in multiplicative estimation—can lead to extremely low compound estimates of risk. This is significant because while a bias of one order of magnitude in central tendency appears minor, the presence of several such biases in sequence will shift final results by many orders of magnitude.

Finding 8: The uSSRA does not describe the approaches used to ensure thoroughness in the review of parametric inputs. It is impossible to determine whether the scientific literature and other information used to support risk assessment assumptions have been thoroughly reviewed and evaluated. Many parameter estimates depend on outdated references or on only a single reference. At times, the uSSRA selects the lowest resulting risk input factors despite the availability of other data yielding higher risk.

Finding 9: The uSSRA has improved its epidemic modeling to address previous criticisms; however, there continue to be significant limitations in model capabilities and available data, leaving large uncertainties in the numbers provided. Particular assumptions likely led to an underestimation of the magnitude of spread and the duration of an FMD outbreak that would result from an FMDv release from the NBAF in Manhattan, Kansas.

Finding 10: Although the methods used for the economic analysis are appropriate, the uSSRA does not provide sufficient information to replicate the results or to assess whether the analysis was properly executed. Underestimates of the magnitude, spread, and duration of an FMD outbreak were carried over into the economic model and led to a likely underestimate of the economic consequence of an FMDv escape from the NBAF.

Finding 11: The committee questions the conclusion that catastrophic natural hazards pose the greatest risk for accidental release of FMDv and finds that the uSSRA overestimates their probabilities. Despite

eastern Kansas being a region of relatively low seismicity, the uSSRA designates earthquakes as the hazard most likely to lead to an FMDv release from the Manhattan, Kansas, facility. One reason for DHS's conclusion is that the uSSRA uses an annual exceedance probability of a 1-second ground shaking as the defining hazard, whereas a low-rise structure like the NBAF is mostly susceptible to a shorter period event. This results in an exceedance probability that is higher by perhaps a factor of 20 than what should have been used and inflates the earthquake hazard risk estimates. Furthermore, the uSSRA does not account for the low structural fragility (strong resistance) of the proposed design, so the probability of a release is overestimated by perhaps several orders of magnitude.

For tornado loading, the hazard is estimated (e.g., probability of exceedance of tornado winds above certain speeds), but again the facility's low structural fragility to those winds is not considered. That leads to overestimation of the risk of releases due to tornadoes by implicitly assuming that any wind event above a particular speed leads to a release of 100% of the material available for release. Thus, the committee considers the estimates of the probability of releases due to both natural hazards to be too high.

Finding 12: The uSSRA is based on assumptions about surveillance, detection, response, and mitigation strategies that were not adequately comprehensive or science-based. Also, it appears they were developed with insufficient input from stakeholders and federal, state, and local governments. Assumptions used to model mitigation, response, and detection were based in large part on DHS and USDA expectations for significantly improved plans, programs, and strategies that would be implemented by the time the NBAF opens in 2020. Surveillance, detection, and emergency response capabilities (such as vaccine availability) are critical for mitigating an outbreak; yet those tools and capabilities are currently limited or not in place. There was no indication from DHS or USDA that the necessary science-based capabilities noted by the previous committee (see Finding 7 of 2010 NRC report *Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas*) would be implemented for FMD surveillance and response.

DHS and USDA still have significant gaps for providing these critical capabilities and for realistically carrying out plans that identify and incorporate agricultural, animal health, and public health sectors and major issues related to a potential pathogen release. If these assumed plans, programs, and strategies are not fully developed, validated, and implemented by the time the NBAF opens in 2020, the risks and con-

sequent impacts will likely be substantially greater than estimated in the uSSRA.

Finding 13: The uSSRA does not adequately address plans for personnel preparedness and training at the NBAF. Although the training and preparedness requirements of the Federal Select Agent Program established under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 are well documented, the uSSRA fails to include the DHS plans for personnel training in security, laboratory procedures, and emergency response as required by P.L. 112-10. Those plans are critical for ensuring safe operations at the NBAF and for mitigating an accidental FMDv release from the laboratory. Exclusion of such information from the uSSRA leads the committee to believe that preparations for the requirement have not been fully addressed by DHS.

Finding 14: In the BSL-4 assessment, the uSSRA does not consider overall risk and presents a limited qualitative assessment of impact. Such an evaluation likely underestimates the overall risk related to the BSL-4 suite, and the potential impact of a release cannot be evaluated. The committee recognizes the inherent limitations in the available information regarding the henipaviruses that form the basis of the BSL-4 review and other agents that may be studied in the BSL-4 suite. However, the risk assessment presented focuses only on the *unique* risks of release from the BSL-4 suite associated with use of large animals. As a result, the approach used for the BSL-4 evaluation understates the range of potential risks in the BSL-4 environment.

LIMITED APPLICABILITY OF THE UPDATED SITE-SPECIFIC RISK ASSESSMENT

For any risk assessment, results apply only when the assumptions upon which they are based are consistent with practice. The uSSRA makes key assumptions about the physical design of the facility, maintenance and operation, and implementation of mitigation strategies. Any significant deviation from the assumed characteristics will modify risk factors and reduce the validity of the risk assessment.

It is critical to recognize that a sufficient level of funding for the NBAF and for risk mitigation activities is required to carry out the planned assumptions noted in the uSSRA. Operating BSL-3 and especially BSL-4 facilities is expensive because of equipment, personnel, operating costs, and maintenance and because of the need for systems for detection and active surveillance. Shortcomings in any of those areas will impact the risk profile

of the facility. Without a long-term funding commitment that is sufficient to maintain the level and quality of NBAF operations and that can sustain planned mitigation strategies, the findings presented in the uSSRA are not assured.

Not all deviations from the planning assumptions would significantly alter risk. If the uSSRA had included a careful sensitivity analysis based on alternative assumptions and if the deviations had been captured in such a sensitivity analysis, the uSSRA might still be applicable. The uSSRA provided to the committee contains no such sensitivity analysis. The uSSRA has limitations in its applicability, and these limitations are not clearly stated in the uSSRA. Absent a thorough sensitivity analysis, the applicability of the uSSRA under alternative operational conditions cannot be ascertained.

CONCLUSIONS

It is important to note that research, diagnostic, and mitigation capabilities envisioned for the NBAF are critical for protecting the nation against known threat agents along with emerging and unknown disease threats. The present committee echoes the conclusions of previous NRC committees that the United States needs the capacity to support critical research and diagnostic programs for the study of foreign animal diseases and zoonotic diseases that are directly linked to securing the health and wealth of the nation.

As required by P.L. 112-10, the committee was instructed to judge the adequacy and validity of the uSSRA. The committee has identified serious concerns about (1) the misapplication of methods used to assess risk, (2) the failure to make clear whether and how the evidence used to support risk assessment assumptions had been thoroughly reviewed and adequately evaluated, (3) the limited breadth of literature cited and the misinterpretation of some of the significant supporting literature, (4) the failure to explain the criteria used to select assumptions when supporting literature is conflicting, (5) the failure to consider important risk pathways, and (6) the inadequate treatment of uncertainty. Those deficiencies are not equally problematic, but they occur with sufficient frequency to raise doubts about the adequacy and validity of the risk results presented. In most instances (e.g., operational activities at the NBAF), the identified problems lead to an underestimation of risk; in other instances (e.g., catastrophic natural hazards), the risks may be overestimated. As a result, the committee concludes that the uSSRA is technically inadequate in critical respects and is an insufficient basis on which to judge the risks associated with the proposed NBAF in Manhattan, Kansas.

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Introduction

Safeguarding U.S. agriculture from foreign animal diseases[1] and protecting our food system require cutting-edge research and diagnostic capabilities. The Department of Homeland Security (DHS) and the U.S. Department of Agriculture (USDA) have embarked on a mission to fulfill Homeland Security Presidential Directive 9 (HSPD-9) to enhance U.S. capabilities since that directive was issued by President George W. Bush in 2004. HSPD-9, *Defense of United States Agriculture and Food*, 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." In response to HSPD-9, DHS plans to replace the aging Plum Island Animal Disease Center by constructing and operating a new facility, the National Bio- and Agro-Defense Facility (NBAF).

UNIQUE CAPABILITIES AND RISKS ASSOCIATED WITH THE NATIONAL BIO- AND AGRO-DEFENSE FACILITY

The NBAF is envisioned and designed as a state-of-the-art high-biocontainment facility that the nation and others would rely on for re-

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

search in and diagnostics of foreign animal diseases and zoonotic diseases.[2] It would serve as a critical world reference laboratory for identifying emerging and unknown disease threats and thus would be an important asset for securing the health, wealth, and security of our nation.

As noted by the previous National Research Council committee that evaluated the DHS site-specific risk assessment (SSRA) in 2010, the planned NBAF would bring new capabilities and risks for the United States (NRC, 2010). First, locating the NBAF in Manhattan, Kansas, demonstrates an important U.S. policy and philosophy shift regarding the conduct of foot-and-mouth disease (FMD) research on the U.S. mainland. The United States has been free of FMD since 1929 (USDA-APHIS, 2007), and research on live FMD virus[3] (FMDv) has not been permitted on the U.S. mainland since 1937[4] because it is a highly infectious viral disease of cloven-hoofed animals and constitutes a major threat to the livestock industry. Second, the NBAF would conduct substantial research and training activities with large animals that are infected with biosafety level 4 (BSL-4)[5] pathogens, which would be important for understanding zoonotic diseases. Having BSL-4 capabilities for large animal research will be critical as new and unknown threats emerge. When operational, the NBAF would be the world's fourth facility to have BSL-4 laboratories capable of large animal research: the others are in Geelong, Australia; Winnipeg, Canada; and Insel Riems, Germany. The one in Germany is undergoing laboratory commissioning as of this writing (Thomas Mettenleiter, Friedrich-Loeffler-Institut, personal communication, May 11, 2012).

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[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, thus preventing the efficient production of food animals and creating obstacles for the international trade of animals and animal products (WHO, 2012; IOM and NRC, 2009).

[3]Foot-and-mouth disease virus is a BSL-3 agent. *Biosafety in Microbiological and Biomedical Laboratories (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 FMDv) that present a risk of causing great economic harm if they infect the indigenous animal population (NRC, 2005).

[4]In accordance with 21 USC Section 113a, live FMDv is not permitted on any part of the mainland of the United States unless the Secretary of Agriculture permits otherwise.

[5]*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).

PROPOSED SITE IN MANHATTAN, KANSAS

The proposed site of the NBAF is on the Kansas State University campus in Manhattan, Kansas, in Riley County. The NBAF will border the Biosecurity Research Institute and will be adjacent to the College of Veterinary Medicine. Kansas is in an area designated as Tornado Alley because of its disproportionately high frequency of tornadoes (NOAA, 2012). Kansas is not especially prone to earthquakes, although the Humboldt Fault Zone runs east of Manhattan (USGS, 2012). The updated SSRA (uSSRA, p. 215) notes that the location selected for the NBAF is not susceptible to flooding. As acknowledged in the 2010 SSRA and the uSSRA, about 10% of the nation's cattle population reside within a 200-mile radius of Manhattan, Kansas (USDA-NASS, 2009)—and approximately 45% of the nation's cattle reside in the 7 states that were modeled as the expected impact area in the uSSRA (USDA-NASS, 2011)—which makes the region a major hub for transportation of cattle and other livestock for the entire United States.

PREVIOUS ASSESSMENTS

The site-selection process for the NBAF began in January 2006. DHS prepared an environmental impact statement (EIS) and a threat risk assessment for the six sites under final consideration (DHS, 2008). On the basis of those studies, DHS selected Manhattan, Kansas, as the location for the new NBAF in January 2009 (74 Federal Register, 2009).[6] The Government Accountability Office subsequently raised concerns about the methods used in the EIS to determine risks for conducting FMDv research on the mainland and also found the EIS analyses to be flawed in determining the economic costs of an FMD outbreak (GAO, 2008, 2009). As a result, the FY 2010 DHS Appropriations Act (P.L. 111-83) mandated that DHS conduct a site-specific biosafety and biosecurity mitigation risk assessment (the 2010 SSRA) for the NBAF at the proposed Manhattan, Kansas, site; required the National Academy of Sciences (through its operating arm, the National Research Council) to independently evaluate the SSRA; and prohibited obligation of NBAF construction funds until the evaluation was complete. In 2010, a National Research Council report found that the SSRA had many legitimate conclusions but that it was not entirely adequate or valid, because of flawed methods and assumptions that underestimated the risks and economic costs associated with an accidental FMDv release from the Manhattan site (NRC, 2010). The findings of that report are presented in Box 1-1.

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[6]Available online at http://www.gpo.gov/fdsys/pkg/FR-2009-01-16/pdf/E9-914.pdf (accessed March 23, 2012).

Box 1-1
Findings of the 2010 National Research Council
Review of the DHS Site-Specific Risk Assessment
for the National Bio- and Agro-Defense Facility

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.

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.

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.

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.

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

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

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.

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.

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.

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.

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

SOURCE: NRC, 2010.

CONGRESSIONAL MANDATE AND STATEMENT OF TASK

As a result of concerns raised in the 2010 National Research Council review, the FY 2011 Department of Defense and Full-Year Appropriations Act (see Box 1-2) mandated that DHS revise its SSRA to address shortcom-

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Box 1-2
Department of Defense and Full Year
Continuing Appropriations Act, 2011

Public Law 112-10, Sec. 1647.

(a) Section 560 of Public Law 111-83 shall not apply to funds appropriated by this division.

(b) No funding provided in this division shall be used for construction of the National Bio- and Agro-defense Facility until the Department of Homeland Security has, pursuant to the schedule submitted by the Department of Homeland Security on March 31, 2011, to the Committees on Appropriations of the Senate and House of Representatives—

(1) completed 50 percent of design planning for the National Bio- and Agro-defense Facility, and

(2) submitted to the Committees on Appropriations of the Senate and the House of Representatives a revised site-specific biosafety and biosecurity mitigation risk assessment that describes how to significantly reduce risks of conducting essential research and diagnostic testing at the National Bio- and Agro-defense Facility and addresses shortcomings identified in the National Academy of Sciences' evaluation of the initial site-specific biosafety and biosecurity mitigation risk assessment.

(c) The revised site-specific biosafety and biosecurity mitigation risk assessment required by subsection (b) shall—

(1) include a quantitative risk assessment for foot-and-mouth disease virus, in particular epidemiological and economic impact modeling to determine the overall risk of operating the facility for its expected 50-year life span, taking into account strategies to mitigate risk of foot-and-mouth disease virus release from the laboratory and ensure safe operations at the approved National Bio- and Agro-defense Facility site;

(2) address the impact of surveillance, response, and mitigation plans (developed in consultation with local, State, and Federal authorities and appropriate stakeholders) if a release occurs, to detect and control the spread of disease; and

(3) include overall risks of the most dangerous pathogens the Department of Homeland Security expects to hold in the National Bio- and Agro-defense Facility's biosafety level 4 facility, and effectiveness of mitigation strategies to reduce those risks.

(d) The Department of Homeland Security shall enter into a contract with the National Academy of Sciences to evaluate the adequacy and validity of the risk assessment required by subsection (b). The National Academy of Sciences shall submit a report on such evaluation within four months after the date the Department of Homeland Security concludes its risk assessment.

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ings, required the National Academy of Sciences (through the National Research Council) to evaluate the uSSRA, and prohibited obligation of construction funds until the completion of another risk assessment. The scope for both the 2010 SSRA and the 2012 uSSRA addressed accidental release of pathogens from the NBAF in Manhattan, Kansas, and excluded terrorist acts and malicious threats from its risk assessments. This report represents the National Research Council's response to the charge as elaborated and delineated in the committee's statement of task (see Box 1-3).

Box 1-3
Statement of Task

The National Research Council will convene a committee of experts to review a congressionally mandated, updated site-specific risk assessment (SSRA) conducted by the Department of Homeland Security for the planned National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas. The Updated SSRA will be prepared in response to the Department of Defense and Full-Year Continuing Appropriations Act of 2011 (P.L. 112-10, Sec. 1647), which requires that it address concerns previously raised in an NRC review of the initial site-specific risk assessment for the NBAF, and requires that it describe risk reduction and mitigation strategies related to conducting essential research and diagnostic testing at the NBAF.

DHS will provide the committee with a presentation on the contractor's approach for developing the work plan for the updated SSRA. Committee members and other meeting participants will discuss gaps in the DHS-presented approach, credible approaches and options to consider for the risk assessment, and areas where further technical input and assistance is needed. Based on those discussions, the committee will organize a workshop to include presentations with invited technical experts, and the workshop will serve as an information-exchange forum to address various issues raised by the DHS-presented approach. At a subsequent meeting, DHS will provide draft sections of the updated SSRA for committee members and other participants to discuss any remaining gaps or additional approaches to consider for the final updated SSRA. There will be discussion of issues from individual committee members and other participants, but no consensus advice will be provided from these open-session meetings.

Following the completion of the final updated SSRA, the committee will review the document and prepare a report to DHS and Congress containing its findings on the adequacy and validity of the final updated SSRA. The report will be provided to the sponsor within 4 months of receiving the final updated SSRA from DHS. 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 final updated SSRA.

COMMITTEE'S APPROACH TO ITS TASK

Information Gathering Meetings

The National Research Council convened a committee of experts to evaluate the uSSRA for the NBAF in Manhattan, Kansas (see Appendix A for committee biosketches). On September 6–7, 2011, the committee organized a workshop and invited experts to join the committee in discussing DHS's proposed approaches for revising the SSRA. On November 8, 2011, DHS briefed the committee on the updated 65% design phase plans for the NBAF. On January 27, 2012, members of the committee held a meeting at Kansas State University in Manhattan, Kansas, to discuss the community's expectations regarding collaborative research and preparedness with the NBAF and to hear comments from the public (see Appendix B for meeting agendas and attendees). Members of the committee also visited the proposed NBAF site and toured facilities at Kansas State University's College of Veterinary Medicine and at the Biosecurity Research Institute.

DHS delivered the uSSRA final report consisting of three volumes to the committee on February 10, 2012. The committee convened on March 16, 2012, in Washington, DC, to discuss it with DHS and its contractors. In March 2012, the committee submitted clarification questions to DHS, and DHS provided written responses and additional materials to the committee that are available as an addendum to the uSSRA.

Process for Determining Adequacy and Validity

The committee used various approaches in evaluating the adequacy and validity of the uSSRA. First, the committee examined whether the uSSRA's methods and statements were consistent with and supported by current acceptable scientific thinking, methods, and findings. Second, for approaches in the uSSRA that were inconsistent with generally accepted practices or approaches and for approaches that had not been previously assessed through scientific peer-review and publication processes, the committee exercised its judgment based on the quality of reasoning, soundness of logic, and strength of support in the existing body of scientific literature and knowledge. Third, the committee assessed the clarity and precision of the analysis provided in the uSSRA. Finally, the committee reviewed whether the uSSRA addressed shortcomings raised in the previous committee's evaluation (NRC, 2010).

Limitations of the Scope

The statement of task outlines a narrow yet definitive scope for the committee's report, which is limited to assessing the scientific adequacy and validity of the final uSSRA provided by DHS. It was beyond the purview and expertise of the committee to judge the selection of Manhattan, Kansas, as the site of the NBAF. In addition, the committee was not asked to provide its own risk assessment in the short 4-month timeframe provided for the review.

ORGANIZATION OF THE REPORT

In the remainder of the report, the committee evaluates the uSSRA and presents its findings and conclusions. Chapter 2 provides an evaluation of the NBAF designs, operations, and response planning. Chapter 3 examines the risk approaches and calculations used in the uSSRA. Chapter 4 evaluates the methods and assumptions provided in the uSSRA to model events that could lead to an accidental release. The committee assesses the methods, assumptions, and analysis used in the uSSRA for the fate and transport model, the epidemic model, the economic model, and BSL-4 assessment in Chapters 5, 6, 7, and 8, respectively. Chapter 9 presents an overall assessment and includes the committee's findings and conclusions.

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2

Evaluation of Design, Operations, and Response Planning as Related to the Risk Assessment

DESIGN PLANS

The updated site-specific risk assessment (uSSRA) of the National Bio- and Agro-Defense Facility (NBAF) indicates that design modifications have been incorporated in the 65% design planning phase to enhance the facility's overall biosafety and biosecurity. Members of the committee reviewed the facility's 65% design phase documents to understand the assumptions about the release probabilities for the uSSRA and to verify that design concerns and recommendations raised by the previous National Research Council committee (NRC, 2010) had been adequately addressed. However, it was beyond the committee's task to formally review or pass judgment on the actual engineering of the facility. Therefore, the comments provided below are not to be construed as an evaluation of the safety of the facility.

Members examined the plans and specifications, verified the presence of critical system components, and determined that calculations on waste streams were conservative. Many design solutions used and validated in the latest generation of high- and maximum-biocontainment facilities had been adopted and in some cases improved upon in the NBAF 65% design plans—an indication that some important lessons learned were incorporated during the design process. Committee members identified process flows for the entry and exit of materials, personnel, and animals and determined that they were logical and well conceived. In this context, design issues raised by the previous committee (NRC, 2010) were addressed in the 65% designs. The committee concurs with the uSSRA that design elements can enhance the safety of the biosafety level 3 agriculture (BSL-3Ag) and

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BSL-4 areas, and can reduce the risk of release of high-containment pathogens in aerosol, solid, and liquid waste streams.

STANDARD OPERATING PROCEDURES, PERSONNEL TRAINING, AND EMERGENCY RESPONSE PLANNING

The committee recognizes that the uSSRA has made substantial advances over the 2010 SSRA in describing how the NBAF would develop standard operating procedures, personnel training, and emergency response planning. The uSSRA mentions future plans to further describe in detail, finalize, and operationalize such plans, policies, and procedures once the facility designs and construction have matured. Although the training and preparedness requirements of the Federal Select Agent Program established under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 are well documented, the uSSRA does not include the Department of Homeland Security (DHS) plans for personnel training in security, laboratory procedures, and emergency response as required by P.L. 112-10. Omission of that information from the uSSRA leads the committee to believe that preparations for this requirement have not been fully considered by DHS.

The content of the uSSRA suggests that BSL-3 and BSL-4 laboratories similar to the NBAF (such as those at Pirbright, UK, and Winnipeg, Canada) were queried for insight into standard operating procedures, personnel training, and emergency response planning. That is a substantial step beyond what was provided in the 2010 SSRA. However, many facilities in the United States, both federally and privately funded, work with select agents under the same regulations that the NBAF will have to operate under, and they could have provided additional insights into lessons learned, best practices, and the other issues addressed in the uSSRA.

The uSSRA provides a detailed list of emergency response best practices drawn from international, federal, and Kansas state resources to inform NBAF preparedness efforts. Absent from the list to draw upon for best practices are the National Fire Protection Association Standard on Disaster/ Emergency Management and Business Continuity Programs (NFPA 1600) and the Emergency Management Accreditation Program Standard, both of which provide current accepted practice information for emergency management programs. The uSSRA did not mention that Riley County has achieved National Weather Service StormReady status, an important achievement in all hazards and severe weather preparedness.

Overall, the conclusion reached in the uSSRA is that more efforts will be required in the future to develop and implement standard operating procedures, personnel training, and emergency response planning. Additional information will need to be obtained from all relevant sources to

fully inform the NBAF operators of the risks in order to optimize plans and procedures. Such relevant resources for key information include DHS's National Biodefense Analysis and Countermeasures Center, the National Institute of Allergy and Infectious Diseases's Regional Biocontainment Laboratories and National Biocontainment Laboratories, the Department of Defense's U.S. Army Medical Research Institute for Infectious Diseases, the Centers for Disease Control and Prevention, and other publicly and privately funded containment laboratories. Operators, scientists, biosafety officers, and response personnel from those facilities could offer significant insight into threats and hazards, lessons learned, crisis communication, and operations concerns to more fully inform those for the NBAF. Similarly, Riley County uses a hazard vulnerability analysis tool, which provides the best overarching view of the threats judged to pose the greatest risks to the county because of their probability of occurring, various vulnerabilities that exist in the area, and the consequences to people, property, the environment, and other assets (Patrick Collins, Riley County Emergency Management, personal communication, February 17, 2012). That may be instructive for the NBAF risk management and emergency planning process. The uSSRA indicates that these three critical areas will be addressed in the future when the NBAF begins construction and when it is closer to being operational. This raises the possibility that risks that needed to have been considered were never actually considered or modeled as part of the current risk assessment and which might be uncovered or recognized in the future.

REFERENCE

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3

Evaluation of Risk Approach and Calculations

RISK MODELING FRAMEWORK

The updated site-specific risk assessment (uSSRA) of the proposed National Bio- and Agro-Defense Facility (NBAF) uses a quantitative modeling framework. That is an important advance over the 2010 SSRA. The framework includes the identification of risk scenarios, calculation of event likelihoods as annual frequencies of occurrence, assessment of consequences of an infection event, calculation of annual expected consequences, total calculation of risk of all events, and uncertainty analysis.

APPLICATION OF RISK METHODS IN THE UPDATED SITE-SPECIFIC RISK ASSESSMENT

The modeling framework is a "scenario-based" approach that is well established for analyzing risk in complex systems. It is a solid method. However, the committee identified issues of concern in how the framework was implemented. Some of the concerns have broad implications for the adequacy and validity of the report. The uSSRA adopts the contemporary terminology of ISO 31000 in describing the modeling framework, which is to be commended; but inconsistencies in the presentation of the method and in the use of terminology make it at times difficult to understand how the methods were applied.

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Risk Metric

Defining risk as an expected (probability weighted) consequence is consistent with current practice, but this metric masks the difference between high-probability/low-consequence events and low-probability/high-consequence events. That approach is not incorrect, but a preferred and more informative metric would be the probability–consequence "risk curve" in which various levels of consequence (C_{event}) are plotted against corresponding probabilities (P_{event}) (Cox, 2009). Although this is not a fundamental flaw in the chosen approach, presenting outcomes in the more informative way would have provided richer information to the reader.

The Logic Modeling Approach

The uSSRA uses a non-binary event tree modeling technique, which is appropriate and standard present practice. Whereas the technique seems to be correctly applied, it is difficult to understand the analysis and its results. The uSSRA uses fault tree symbols at branch points of the event trees, which is confusing and suggests a poor understanding of basic terminology. The uSSRA incorrectly refers to the event trees as fault trees in most cases but refers to them as event trees in others.

Typical risk scenarios in the report involve a temporal sequence of events; therefore, an event tree approach is effective for enumerating all possible chains of events in a scenario. In modeling failure of system components, however, a fault tree approach provides a better way of capturing system failure paths (e.g., minimal cut sets) than the event tree approach (Cox, 2009). For this reason, many industrial installations use risk analyses that are a hybrid of event trees and fault trees (Cox, 2009). The uSSRA should have followed suit by using a hybrid model, but it did not.

Mean Versus Median

The uSSRA lacks a consistent approach to calculating middle values or best estimates. Most of the risk calculations use the estimated 50th percentile (the median); some use the mean (for example, see discussion on Q values on p. 578 of the uSSRA). The median and mean can differ by orders of magnitude in highly skewed distributions, which appear to be the case for many parameters in the risk calculations. A consistent approach should have been used in the uSSRA, and it should have relied upon the mean rather than the median.

Implied and False Precision

The uSSRA provides estimates that do not appropriately consider significant figures; this was also a concern noted by the previous committee (NRC, 2010). As the present committee noted in its March 2012 public meeting, carrying more than one digit in calculations, where values of input parameters vary by many orders of magnitude, implies more precision than is possible. Rounding to one digit would have been appropriate.

SPECIFIC CROSS-CUTTING ISSUES

The committee identified several issues in how the uSSRA carries out the risk assessment that would apply to the various event calculations and affect the overall estimates. The notable ones are related to rates of human error, sensitivity and uncertainty analysis, and probabilistic dependency.

Treatment of Human Error

Many scenarios identified in the uSSRA include human error. The uSSRA uses a generic probability of human error for most cases "based on human reliability assessments for highly reliable and trained workers such as those to be employed at the NBAF" (p. 139). It mostly adopts a value of 5×10^{-3} for failure per error opportunity, which is based on human error probabilities suggested for nuclear power industry applications (Spurgin, 2009). The uSSRA states that this failure probability is used for any mitigating systems or event nodes that are dependent upon a worker performing an action.

The committee finds the uSSRA's treatment of human error inadequate. There is no evidence of a rigorous NBAF-specific human reliability analysis, which is a necessary component that is found in comprehensive risk analyses (U.S. NRC, 2005). Values for human error rates in work settings similar to the NBAF should be based on related empirical evidence. From the text provided in the uSSRA, the human error rate does not appear to be based on a rigorous and transparent analysis of the available data for similar operations. The human error rate of 1 in 200 and lower for "highly skilled workers" seems to have been arbitrarily selected and indiscriminately applied.

With the NBAF designs at only 65% completion, it may seem premature to develop human error probabilities that are site-specific and task-specific. Nevertheless, it is the responsibility of DHS and its contractors to provide such estimates for human error probabilities as part of the uSSRA. This could have been done given the available information about the site,

the general understanding of tasks involved, the experience of other laboratories, and the nature of a human role in the risk scenarios.

In at least one pathway, the uSSRA uses an unrealistically low value of 2×10^{-4} of failure per error opportunity for human error that is not justified in the report. The uSSRA claims that NBAF workers would be more highly skilled than "skilled workers" and provides an error rate of 5×10^{-3} of failure per error opportunity with no further substantive explanation.

It was critical for the uSSRA to have explored possible sources of data and operating experience related to human errors in research laboratory settings as the basis of generic or reference error probability. Rates of error in various types of tasks similar to those involved in a facility of the NBAF type are provided by Kletz (2001), and are all much higher than the values used in the uSSRA. Data from the U.S. Department of Agriculture and Centers for Disease Control and Prevention's (CDC) annual *Reports to Congress on Thefts, Losses, or Select Agents or Toxins* may provide somewhat better information, but even such information would be based on mature operations that have been in practice for years at established facilities with experienced, integrated cores of workers, supervisors, and management. The NBAF's large-animal capabilities will introduce unfamiliar operational risks. An analysis of the experience of the most similar operations—such as those at Pirbright, UK, Geelong, Australia, and Winnipeg, Canada, for comparable foreign laboratories, and the U.S. Army Medical Research Institute of Infectious Diseases, CDC, and University of Texas Medical Branch at Galveston for comparable U.S. laboratories—may provide more informative guidance than the apparently arbitrary assumption of human error rate used in the uSSRA.

The uSSRA does not account for the possibility that routine tasks can be associated with high failure rates even when carried out by highly trained workers. For example, in 2004, at least three researchers were exposed to and later developed tularemia when they handled a live rather than avirulent strain of the bacteria (Lawler, 2005). That event investigation revealed that researchers routinely failed to comply with safety and other protocols (Barry, 2005). In another case in early 2004, highly skilled workers shipped an anthrax sample that was supposed to be heat-killed but instead was alive and thereby exposed the recipients to anthrax (Enserink and Kaiser, 2004). Also in 2009, a military scientist who worked with cultures of tularemia bacteria was infected and developed symptoms of the disease; it took at least two weeks for the disease to be properly diagnosed (Eckstein, 2009).

The following are examples of the inappropriate treatment of human error in the uSSRA at several key events in mitigation pathways:

- *System failure rates*. Rates of system failure, such as failure of a cook tank to function properly to kill foot-and-mouth disease virus

(FMDv), are based generally on the notion that the system has been properly operated and maintained in accordance with a vendor's claims (see additional discussion of cook tank failure later in this chapter). Inadequate operation or maintenance (human error) are not considered in the uSSRA.

- *Disinfectant failure.* The use of expired disinfectants or failure to apply disinfectant properly (human error) are not calculated in the event tree design.
- *Efficiency of showering.* Efficiency of showering to remove virus on the body is given as 81–98%, but the scenario tree does not include possible human errors in not following protocol for showering.
- *Transference (contact, fomite).* The event tree in Figure 4.5.1-8 (p. 160 of the uSSRA) assumes that employees will always submit rings, eyewear, etc. for disinfection. The uSSRA assumes that certain procedures would prevent such items from entering animal-handling rooms (AHRs). Human error in neglecting to acknowledge or disinfect these fomites is not included.
- *Necropsy transference.* An error consistently found in the event tree pathways involves omission of an acknowledgment or observation of an event, such as failing to notice a leaking glove, an inappropriately fitting respirator, or a spill or leak. Failure to include this type of human error, referred to as slip error, would in essence mean that the model assumes the slip error rate to be zero.

Sensitivity and Uncertainty Analysis

A critical part of risk analysis is characterizing the uncertainty in the results and the sensitivity of those results to changes in assumptions or parameter values. The importance of uncertainty analysis has been recognized since the early era of quantitative assessment of health, safety, and environmental risks in federal practice, and this has been expounded in a series of National Research Council reports on risk analysis (e.g., NRC, 1983, 1994, 2009).

Uncertainty in risk analyses is usually divided into two types: uncertainties due to natural randomness and uncertainties due to limited knowledge, which are referred to as *aleatory* and *epistemic*, respectively. Aleatory uncertainty refers to the inherent or natural variations in the physical world (NRC, 1996, 2000). Epistemic or knowledge uncertainty refers to scientific uncertainty due to lack of data or knowledge about real-world events (NRC, 1996, 2000). A model and its parameters may include aspects that have great scientific certainty and well-defined aleatory variability. The model and parameters may also include aspects with a high degree of scientific uncertainty and with a differing extent of variability.

The uSSRA mentions epistemic and aleatory sources of variability and

uncertainty in the risk assessment (p. 15). However, the statement that "modeling data included a thorough treatment of uncertainty, including both aleatory and epistemic, to provide a reasonable range of possible outbreak risks" is not supported in the text. In some sections of the uSSRA, some pieces are provided as a good start particularly for the sensitivity analysis, which covers mainly the aleatory variability but also some aspects of epistemic uncertainty (for example, see pp. 534–539). But even in that specific example, the sensitivity analysis examines the impact of a 0.5- to 2-fold change in parameter values that actually have far greater ranges between "low," "median," and "high"—at times 6–9 orders of magnitude.

It is unclear whether a consistent approach was used throughout the uSSRA for expressing uncertainty in input parameters. More specifically, the committee could not determine whether low, medium, and high values of some parameters represent corresponding percentiles of a continuous (or discrete) probability distribution. As previously mentioned, this is complicated by the fact that the middle value of the range is sometimes referred to in the report as the mean and in other occasions as the median. Both are meaningful only in the context of a probability distribution, and the distributional assumptions for the input parameters are unclear.

A major concern regarding the treatment of uncertainty is exemplified in how the point estimate and uncertainty distributions are calculated for P_i (the conditional probability of infection). The approach is described on p. 579:

> *Regardless of the pathway, for each event a separate estimate for P_i is computed for each Q value (Q_L, Q_M, and Q_H). The resulting conditional probabilities are listed as: P_{iL}, P_{iM}, and P_{iH}. The value P_{iL} is associated with Q_L, which represents the 5th percentile of possible Q values associated with a given loss-of-containment outcome. In other words, 5% of the time that a loss of containment occurs, the amount of FMDv involved in the release will be Q_L or less and the probability of an infection event is P_{iL}. Similarly, 5% of the time that a loss of containment occurs, the amount of FMDv involved in the release will be Q_H or higher and the probability of an infection event is P_{iH}. The remaining 90% of the time that a loss of containment occurs, the amount of FMDv involved in the release is assumed to be Q_M and the probability of an infection event is P_{iM}. As a result, the estimate for P_i is obtained as follows: $P_i=0.05P_{iL}+0.90P_{iM}+0.05P_{iH}$. The stochastic variability associated with P_i is based on a binomial distribution and is computed as $\sigma_{Pi} = \sqrt{(1-P_i)P_i}$.*

The committee's understanding is that the variable P_i is an event-dependent uncertain quantity subject to at least epistemic uncertainty. Once there is an uncertainty distribution for the variable P_i, there is an associated mean value, $\overline{P_i}$. The distribution of the variable P_i is used in the uncertainty

propagation stage to calculate uncertainty bounds on the total risk. With that understanding, the committee offers the following observations:

• The quantity calculated in the first equation is denoted as $\overline{P}_i$. It seems that through the second equation ($\sigma_{Pi} = \sqrt{(1-P_i)P_i}$) the uSSRA has attempted to develop a distribution for $\overline{P}_i$ presumably for use in uncertainty quantification. As previously stated, the correct quantity that is used in uncertainty quantification is the actual variable P_i and not its mean value $\overline{P}_i$.

• One implication of assumptions behind the calculation of the (mean) P_i in the first equation is that the *variable* P_i is roughly distributed by a three point discrete distribution with 5th and 95th percentiles at P_{iL} and P_{iH}, respectively. Based on the above discussions, the distribution developed based on $\sigma_{Pi} = \sqrt{(1-P_i)P_i}$ not only is a conceptually wrong distribution to use for P_i but is numerically inconsistent with the range indicated by P_{iL} and P_{iH}.

The committee further questions the basis of using a binomial-based "stochastic variability" distribution to capture aleatory or epistemic uncertainty in P_i. Risk analysis methodology dictates that the assessment of uncertainty be based on the nature of the phenomena being considered and on the available information. The committee finds it disturbing that the above approach seems to be how many of the input uncertainty distributions were calculated in the uSSRA, which results in false and in some cases large ranges of uncertainty in the input and output of risk models.

Finally, the committee has concerns about the use of the median of a skewed distribution and its effect on the risk calculations. For instance, many of the Q values have multiple orders of magnitude between the 5th, 50th, and the 95th percentiles. Where the mean falls is difficult to determine without more information. Nevertheless, skewness of one order of magnitude from the median to the mean would alter—when properly using the mean rather than the median—the risk calculations upward by an order of magnitude or more for some factors. Whether or not specific Q determinations have sufficient information to determine the median and the mean, this issue deserves additional attention and resolution. The process of weighting the low, median, and high values continues to propagate the bias introduced in the uSSRA by not considering the possible skewness.

The uSSRA repeatedly mentions that Monte Carlo sampling was used for uncertainty propagation. Monte Carlo sampling is a well-established method, and the committee finds it appropriate for the application. However, the committee could not verify whether the approach was used consistently throughout the uSSRA. In some cases, the uncertainty measures of the output of models (or submodels) appear to have been obtained by

first using the low values of the input parameters to produce the low values of the output parameters, and the same approach was used to produce medium and high input values. Such an ad hoc method may be useful in performing sensitivity analysis to see the effects of compounding extremes but is entirely inappropriate for uncertainty analysis because it produces probabilistically incorrect bounds.

Treatment of Dependencies

It is of fundamental importance in probabilistic modeling to correctly characterize *probabilistic dependencies* among events and model variables and to account for such dependencies in calculating probabilities of the joint occurrence of those events and parameters. The committee finds that the uSSRA ignored potential dependencies in calculating probabilities for the risk scenarios and that this likely resulted in a serious underestimation of the total risk and in incorrect ranking of risk contributors.

A basic rule of the calculus of probability for the joint occurrence of two events E_1 and E_2 is

$$P(E_1E_2) = P(E_2|E_1)*P(E_1)$$

where $P(E_1)$ is the probability of event E_1 and $P(E_2|E_1)$ is the conditional probability of event E_2 given event E_1.

When events E_2 and E_1 are independent, $P(E_2|E_1) = P(E_2)$, and consequently

$$P(E_1E_2) = P(E_2)*P(E_1).$$

Because in many cases $P(E_2|E_1) > P(E_2)$, ignoring potential dependencies can result in significant underestimation of the probability of the joint occurrence of E_1 and E_2. The problem is compounded when more events are involved.

An example of the uSSRA ignoring potential dependencies in risk scenario calculations is in the calculation of the probabilities of biosafety level 3 agriculture (BSL-3Ag) AHR events. In this case and for all other containment areas, the engineered mitigation solutions and expected protocols are designed to provide multiple layers of containment protection and redundancy. According to the uSSRA, all NBAF AHR exhaust systems provide filtration via double high-efficiency particulate air (double-HEPA) in series, multiple failure detection points, and built-in redundancies (p. 144). The filtration and discharge of large volumes of filtered air are provided by dedicated HEPA caissons that provide efficiency (by running in parallel

in nominal conditions) and that accommodate full room exhaust capacity even when one caisson is out of service. The smaller AHRs—Type A, A2 (large), A2 (small), A3, and B—provide full 2N redundancy (complete room air exhaust volume can be accommodated by either HEPA caisson), and the larger AHRs (Types C and D) provide N + 1 redundancy (complete room air exhaust volume can be accommodated with any three of the four caissons).

The uSSRA calculates the probability of Event AA10 as follows: Given the redundancies in filters, if a filter fails (at an estimated P_{Fail} rate of 1.5×10^{-4} failures/year), the redundant pressure alarms (each modeled with a failure probability of 10^{-3} per demand) will initiate the room exhaust redundancy. For one parallel caisson to exhaust unfiltered room air, there would have to be two filter failures, two primary alarm failures, and a redundant alarm failure. Therefore the uSSRA states that the probability of this event is given by

$$P_{event} = (P_{FAIL}{}^*P_{ALARM}{}^* \, P_{FAIL}{}^*P_{ALARM}{}^*P_{ALARM})^2 = 5.06 \times 10^{-34}.$$

Clearly, in that and other similar calculations (such as probabilities of Events AA1 through AA9), the report assumes that failures of the identical filters and identical alarms are independent events.

To illustrate the potential numerical impact of the assumption of independence, the committee applied the beta (β) factor model, which is one of several popular approaches found in the literature (U.S. NRC, 1989a,b) for treating common causes of failures to the probability of Event AA10:

$$P_{event} = \{[(1 - \beta_{FAIL})P_{FAIL}]^4 + \beta_{FAIL}P_{FAIL}\}\{[(1 - \beta_{ALARM})P_{ALARM}]^4 + \beta_{ALARM}P_{ALARM}\}.$$

In this equation the likelihood of failure of system redundancies due to common cause failures is given by βP. Using a generic value of 0.1 for β factors (U.S. NRC, 1989a,b) and the same values of failure probabilities as before, then

$$P_{event} = \{[(1 - 0.1)(1.5 \times 10^{-4})]^4 + (0.1)(1.5 \times 10^{-4})\}\{[(1 - 0.1)(10^{-3})]^4 + (0.1)(10^{-3})\}$$
$$\approx 1.5 \times 10^{-9},$$
$$\text{not } 5 \times 10^{-34} \text{ as given in the uSSRA.}$$

When properly calculated, that probability of 1.5×10^{-9} is 10^{25} times higher than the value calculated in the uSSRA. All other probabilities for Events AA1 through AA9 are also grossly underestimated in the report, and the same error exists for the other pathways.

In failing to address intrinsic and extrinsic dependencies, the uSSRA has grossly underestimated (perhaps by a factor of 10^{25}) the risks of many scenarios for FMDv release from the NBAF that could lead to an outbreak.

INPUT DATA AND PARAMETER ESTIMATES

In several places in the uSSRA, the committee questions the input data and the resulting estimates of an event. Human error inputs are questionable, as previously discussed. Other data inputs that lack sufficient justification or rationale include the following:

1. *Out-of-containment leaks.* The event tree design omitted critical events that could lead to an FMD event by ignoring risk of out-of-containment leaks. These were identified by the previous National Research Council committee as a shortcoming (NRC, 2010). The uSSRA specifically states that only events from the Transshipping Facility and the laboratory will be considered. However, the location of the NBAF in a livestock-rich area necessitates consideration of the conveyance of packages from the Manhattan airport to the Transshipping Facility. Although all biological shipments to and from the NBAF must adhere to International Air Transport Association specifications, it is possible that a shipment destined for the NBAF could be inadequately packaged and result in a serious leak.

2. *Power systems failure.* No scenarios were indicated for power failures, either partial or complete, or for what systems and pathways would be affected and how. Presumably, there would be a correlation between systems events in such a way that a general or partial power failure would affect, at least temporarily, the efficiency of other systems and human error rates. For example, in 2005, the security system and freezers were disabled during a power loss and failure of the back-up electrical system at the CDC Division of Vector-Borne Infectious Diseases in Fort Collins, Colorado (Erickson, 2005), and in 2008, while back-up generators were out of service for upgrades, an electrical outage caused a loss of power to a containment laboratory at the CDC in Atlanta (Young, 2008).

3. *Autoclave failure and incinerator failure.* For both of these probability values, there were no references, and values given were termed "representative."

4. *Disinfectant efficiency.* The uSSRA assumes that disinfectants will be 99.999% efficacious (when used as directed). On the bottom of p. 91 of the uSSRA, it states that a "representative" efficiency of 10^{-1} will be used in modeling *assumptions for disinfectants*, which seems reasonable given heavy organic load and dilution; but later (p. 102), it indicates that 10^{-5} was used, which is contradictory and confusing. The difference is a discrepancy of 10^{-4}. No cited values were given for efficacy under these types of

laboratory conditions. This issue was cited as a shortcoming of the 2010 SSRA by the previous NRC committee.

5. *Cook tank failure.* No efficiency data were provided to support a reduction factor of 10^{-6} for the cook tank. The failure rate for both cook tanks was 10^{-5}, but justification and data were not provided. The probability of partial failure, resulting in loss or partial loss of efficiency, was not indicated.

6. *Glove failure rates and Tyvek suit reduction rates.* No justification was given for the failure rate of unpunctured gloves (10^{-5}) or for Tyvek suit reduction factor of 0.15.

7. *Tissue autoclave and performance indicator failure.* On p. 165 of the uSSRA, there are no references or validations for the values of 10^{-5} for the tissue autoclave and for the performance indicator of the tissue autoclave.

8. *Estimate of FMDv MAR.* Estimates for the amount of FMDv that is aerosolized consider only the amount of virus exhaled by infected animals and fail to consider virus shed in feces, saliva, nares, ruptured vesicles, etc. that is aerosolized by the room ventilation system, hosing and cleaning, and feeding and sampling procedures. The assumed material available for release (MAR) for special procedures, shipment spills, etc. was 3.46×10^4 plaque-forming units per milliliter (PFU/mL) (p. 130). For virus grown in cell culture, the figures mentioned in the uSSRA may be underestimates. Typical virus concentrations are 10^5–10^7 PFU/mL and sometimes 10^8 PFU/mL for cell-adapted virus (Tam et al., 2009). The uSSRA even notes, in discussions of autoclave efficiency, that titers of virus tested were *only* 6.3×10^5 PFU/mL (p. 84).

CONCERNS ABOUT QUANTITATIVE ANALYSIS PRACTICES

A high-quality risk assessment consists of an integrated document that reports consistent information within and between sections. The methods and data need to have sufficient clarity for the results to be reproducible. In many instances, the committee could not verify the uSSRA results, because data and methods were unevenly or poorly presented throughout the document. The committee also struggled with interpretation of critical graphs and tables and was unable to duplicate or reconstruct important risk scenarios, given the information provided.

Use of Terminology

The uSSRA is inconsistent in its use of terminology, and it applies non-conventional graphic representations. For example, it uses the term "fault tree" when it had implemented an event tree throughout its analysis. It

initially uses the term P_{loss} to describe the conditional probability that a loss of containment will occur, given a specific opportunity; this interpretation is then inconsistently applied in other sections, where P_{loss} is used to represent the probability of a particular pathway conditional on the opportunity's occurrence, including pathways where containment succeeds.

Inconsistencies in Figures, Tables, and Text

The uSSRA summarizes important concepts in figures and tables, and these figures and tables are intended to serve as an opportunity to graphically display technically sound and critical information. Some figures and tables are understandable, but others are difficult to interpret, and many captions and legends are unclear. Some examples follow.

Figures

The quantitative information presented in some of the figures in the uSSRA was not immediately obvious to the committee, often because the figures lacked sufficient annotative details. That is exemplified by, but not limited to, Figure 5.1.9-6 (p. 295) and Figures 5.1.10-1 through 5.1.10-6 (pp. 315–322). Furthermore, Figure 4.4.1-1 (p. 118) and Figure 4.4.1-2 (p. 120) may be confusing due to preparation or printing errors. Figures 5.1.8-6 through 5.1.8-11 also would have benefited from more explanation, as would Figures 5.1.10-1 and 5.1.10-2. Occasionally, a caption of a figure does not explain what the figure portrays; an example is Figure 8.2-1, "Frequency-Consequence Plot for All Event Trees," on p. 607.

Another example where information is not clearly provided or misconstrued in the uSSRA is Figure 8.2-2, "Aggregate Risk by Event Tree." The upper error bars are often 3–4 orders of magnitude above the median shown by the top of the colored bars. The uSSRA is deficient in not providing a further discussion, given the uncertainty of many model parameters and the wide range of results. The committee, although limited in the time it spent in tracking the parameters, has concerns that the emphasis on the median in this figure may lead readers to focus on risk that is orders of magnitude lower than is shown by the informative upper percentile results. Moreover, the "error" bars indicated on the graph and in Table 8.2-1 of the uSSRA are incorrectly given as the variance; the proper designation for comparing variation of the point estimates would have been the standard error of the mean.

Tables

Some tables in the uSSRA fail to clearly communicate critical information. Most notably, in Volume 1, Section 4 of the uSSRA (pp. 61–237), the base case (all controls in operation) was identified but can be confused with both the partial control failure and complete control failure pathways. The report would be more reader-friendly if the base case (no control failure) were differentiated and displayed more clearly. Many sections use incorrect or incomplete table headings. In one example, Table 7.4.1-1 of the uSSRA includes the heading "Economic Impacts Summary (Millions)" and subheadings "Producer Surplus" and "Consumer Surplus" (pp. 573–575). Those values could be interpreted as the level of producer and consumer surplus, whereas the text indicates that they are *changes*. The text and Table 7.3.1-9 of the uSSRA that follow immediately appear to provide conflicting information because of inaccurate table headings (p. 563).

Text

The uSSRA is often difficult to follow and verify because of inconsistencies within and between sections. The sections seem to have been composed independently, which is understandable, but the final assembly into one document failed to sufficiently merge the various parts. Referencing is not uniform throughout, and the writing style varies. The committee acknowledges the time constraints in assembling a document of this magnitude, but some lack of cross-referencing created critical holes. For example, the epidemiology section reports a detailed examination of vaccination and depopulation costs that are not incorporated into the economic analysis of the uSSRA (Section 7, pp. 541–576).

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4

Evaluation of Accident Event Modeling

The first step in quantitative risk assessment, as described in the updated site-specific risk assessment (uSSRA), is a description and analysis of the circumstances (accident events) that could lead to release of foot-and-mouth disease virus (FMDv) from the proposed National Bio- and Agro-Defense Facility (NBAF). The purpose of this step is to develop estimates of four critical inputs for the ultimate characterization of site-specific risk. The analysis focuses on the probability and frequency of pathogen release given particular circumstances related to loss of containment and on the amount of pathogen likely to be released. Questions related to the probability that a given release would result in infection and the consequences of such an infection are left to later sections of the uSSRA; the ultimate characterization of FMDv-related risk is presented in Section 8 of the uSSRA.

OVERVIEW OF METHODS FOR ACCIDENT EVENT MODELING

Section 4 of the uSSRA begins with a description and analysis of the pathways that could lead to pathogen release from each of three originating locations within containment and from non-containment areas outside the laboratories. The uSSRA created conceptual models of release pathways and provided estimates of the total amount of material available for release (MAR) from each originating location.

Accident sequences culminate in an event (defined as loss of containment in the uSSRA) that may or may not result in an infection outside the facility. As previously mentioned in Chapter 3, event trees (which are incorrectly called fault trees in the uSSRA) are used to describe the set of

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circumstances leading to release of material. Each node of the event tree (Figure 4.5-1 of the uSSRA) indicates a point in the sequence of events at which a release mitigation system (including human action) either succeeds or fails. "Success" means that the system functions as expected, not that it is 100% effective. An event tree is developed for each originating location and for each of four possible mechanisms, called pathways, by which pathogens could be released (aerosol, liquid waste, solid waste, and transference). This is accompanied by a table that provides the following for each node of the event tree: failure probabilities and "reduction factors" that are to be applied to the MAR, one reduction factor that is assigned when the mitigation system at each event tree node fails, and another when it is fully functional.

The reliability of the ultimate risk estimates presented in Section 8 depends heavily upon the adequacy of the analyses and results from the accident event modeling of Section 4.

COMMENTARY

The method applied in Section 4 is a distinct improvement over that applied in the 2010 SSRA. The use of event tree analysis and probabilistic modeling is preferable to the scenario-based, semi-quantitative approach of the earlier assessment, and is consistent with current risk assessment science for facilities like the NBAF. The adoption of International Organization for Standardization (ISO) Standard 31000 terminology is also to be applauded, although the committee notes some concerns about the misuse of terms.

The committee identified a few significant omissions in the conceptual models used to describe containment and in the elucidation of system failures that could lead to a release (the system failures are summarized in the 24 circumstances presented in Table 4.3.1-1 of the uSSRA). The committee finds that the development of the 142 events that could lead to an infectious or non-infectious release is nearly complete and generally takes into account mitigation systems, including human action, identified in the conceptual models. However, critical issues remain that affect other aspects of the risk assessment, and these are discussed below.

TERMINOLOGY

The uSSRA generally adheres to ISO 31000 terminology. As previously mentioned in Chapter 3, the committee finds that use of the term P_{loss} is confusing, and the uSSRA should have adopted a different term. The uSSRA would be less confusing if the "loss" subscript were dropped, inasmuch as P_{loss} can be easily misread as the probability of loss of FMDv when it carries no such meaning. The term refers to the probability that,

given a specific opportunity, a particular pathway in the event tree will allow release. It includes pathways in the event tree in which all mitigation systems are assumed to be fully functional and pathways in which some mitigation systems fail.

LOGIC ERRORS AND EVENT TREES

Apart from asking subject matter experts for their opinions, no explanation was provided on how the uSSRA selected the 142 events (Appendix Tables A8-1 and A8-2) that were the bases of the event trees. In designing the event trees, several logical circumstances (as indicated by a node) were omitted (i.e., out-of-containment leaks, power systems failures). Thus, the committee is not confident in assuming that all the critical pathways for escape were considered in the uSSRA.

DEVELOPMENT OF FAILURE PROBABILITIES AND REDUCTION FACTORS

It is impossible in the time provided for this evaluation to review every event tree and accompanying table in Section 4 and to comment on the adequacy of the data and assumptions that are used to support all of the large number of estimates of probabilities and reduction factors associated with each of the many nodes of each event tree. Even with a sound method, the reliability of the assessment remains completely dependent on the scientific reliability of each of the hundreds of inputs used.

The committee selected a sampling of event trees and analyzed some of the assumptions and data used to develop estimates for Q, P_{loss}, R_0, and F_{loss}. For each node of at least three event trees, the committee examined the probabilities of failure and success of the mitigation systems and the resulting MAR reduction factors. Such analyses were conducted for events associated with ATR (transference of virus to the respiratory tracts of workers in biosafety level-3 [BSL-3] animal holding rooms), OTB (transference to the body in non-containment areas), and AA (aerosol release from BSL-3 animal holding rooms), and for selected other events.

GENERAL FINDINGS ON DATA INPUTS

Although the uSSRA provided detailed analysis of various risks, the use of questionable assumptions in the data inputs demonstrates that there was insufficient familiarity with the body of scientific literature or with institutional knowledge. The committee believes that this was manifested in citations' being too limited to constitute compelling evidence of support. The uSSRA failed to validate some assumptions through multiple sources

and/or high-quality references. This is evident in how assumptions for data inputs were made; examples of the invalid assumptions are presented below in the case of the aerosol transference pathway and calculations for FMDv. The examples set out in the following are not exhaustive but illustrate the committee's concerns.

Estimates of Material Available for Release

MAR for Aerosol

The committee is concerned that the MAR for aerosolized virus was not adequately estimated. Limited data were applied from two sources which examined exhaled virus of only two serotypes (Alexandersen et al., 2002; Gloster et al., 2008); the uSSRA did not apply data from at least four other studies that found much higher concentrations of aerosol virus (Donaldson et al., 1982; Donaldson and Alexandersen, 2001; Alexandersen and Donaldson, 2002; Alexanderson et al., 2003). Moreover, because of the methods used in the studies cited, the estimates did not account for virus aerosolization from urine, feces, saliva, vesicular fluid, feed dust, etc., and thus the MAR figures for airborne virus would further underestimate actual virus available in the air of animal rooms. Failure to sufficiently consider the broad natural variation in virulence among FMDv serotypes and among strains within a serotype (Beard and Mason, 2000; Mason et al., 2003; Grubman and Baxt, 2004) resulted in overly restrictive and likely unrepresentatively low aerosol MAR estimates for the repertoire of strain–host experiments expected for the NBAF.

MAR for Special Procedures

The MAR assumed for special procedures (e.g., shipment spills) was 3.6×10^4 plaque-forming units per millimeter (PFU/mL) (p. 130 of the uSSRA). The assumed value is low by at least a factor of 100 if one considers the most common type of procedure undertaken daily—namely, virus passage in cell cultures—whether as part of an experiment or simply to maintain the laboratory's inventory of viruses. Specific cell lines are used to maximize the titer of virus, depending on the serotype and strain. Typical virus concentrations are around 10^5–10^7, and sometimes 10^8 for cell-adapted virus (Tam et al., 2009). For determining amounts of FMDv, the uSSRA states that it chose to use only references that involved primary bovine thyroid cells for input data "because the bovine thyroid cell assay is the most sensitive for determining the concentration of FMDv" (p. 110). The only reference cited for that optimal sensitivity dates to 1966 (Snowdon, 1966). However, investigators have been using other cell cultures to grow FMDv for the in-

tervening 45 years with excellent results, and FMDv is now usually grown in BHK or LK cells (of bovine origin) or PK or IBRS2 cells (of swine origin), depending on serotype and other factors. The committee finds that ignoring the intervening literature and basing future practices on a reference from 1966 is a critical oversimplification in stating that only one cell culture is the most sensitive for growing the virus.

More reasonable concentrations would be 10^5–10^7, and occasionally 10^8, depending on serotype and whether it is a primary isolation or a cell-adapted virus. Thus, the use of such a low titer of virus throughout the uSSRA as an estimate for MAR artificially diminishes the magnitude of a leak. Because factors in the model multiply to yield risks, an order-of-magnitude underestimation in each of several multiplied factors quickly reduces the final risk.

Low, Median, and High MAR Values

Accounting for variability in MAR is a valid objective, as is the use of Monte Carlo simulations. The committee notes that many of the input parameters appear skewed and that calculations were completed for the low, median, and high values for MAR (and other factors; see below). These were then assembled by weighting the 5th percentile by 5%, the median by 90%, and the 95th by 5% and taking a weighted sum. That is a purely ad hoc procedure and is inconsistent with the mathematics of probability. If the distribution of values were known, randomly sampling from the whole distribution (rather than separate runs for the 5th, median, and 95th percentiles) would have given more robust insights and allowed for rigorous sensitivity analyses.

Section 4.4.1 of the uSSRA notes that "1,000 runs were performed"; the committee assumes that this refers to the Monte Carlo simulation. Typically, moderately complex models require more than 1,000 or even 10,000 iterations to achieve stability in the output. Without sufficient iterations to give model stability, the results may be inaccurate compared with results based on adequate iterations. The uSSRA should have consistently established that the number of iterations used in Monte Carlo simulations were sufficient to give stable model results, as is standard practice in stochastic modeling. That is, the target error rate and confidence should be specified. Some carefully chosen examples would have improved transparency and clarity of the methods and results.

Assumption About Respirator Use

Regarding lack of sufficient institutional knowledge or practices, the uSSRA states that N95 respirators will always be worn by workers dealing

with animals (alive or dead) that are infected with FMDv (p. 99). The committee suspects that that change in standard operating procedure (SOP) to require respirator use may have been a result of the 2010 SSRA's indicating that the scenario of FMDv transfer without respirators contributed about half the estimated 70% chance of release over 50 years. FMDv investigators at several institutes explored the option of using N95 respirators when working with infected animals and concluded that they were unnecessary (Donaldson, 2008). Inasmuch as animal caretakers routinely go from infected to uninfected rooms the next day, using routine shower and decontamination practices without respirators and without transmitting FMDv to control animals, readers familiar with FMDv would question why N95 respirators would be required and what base of institutional knowledge the uSSRA chose to build from.

The committee also has concerns about the documentation of the sources and reliability of the data used in this analysis. The scientific rationale for wearing respirators presented here is based on studies reported in 1969 and 1970 in which experiments were done to determine the amount of virus present in the nasal passages of humans after exposure to animals infected with FMDv and to determine potential transmission to naïve animals. Those studies are well known to the global FMD community and formed the basis of the 3- to 7-day quarantine period that has been observed at many research facilities working with FMD. However, these studies and assessments were brought into question after the 2001 outbreak of FMD in the United Kingdom: By implementing a policy for an outbreak situation that was intended for the laboratory setting, the mandatory quarantine period so severely restricted the availability of animal health personnel to visit farms that it prompted research after the outbreak. Subsequent experiments done at Plum Island and Pirbright (Amass et al., 2003, 2004; Wright et al., 2010) observed that for a couple of strains, routine biosafety measures, such as showering and changing clothing, were sufficient to keep operators from spreading FMD infection from one animal room to another. The uSSRA does refer to two of the publications dealing with assessment of FMDv carriage by animal health personnel (Amass et al., 2004; Wright et al., 2010) but chooses to compute risk based on much earlier data. Again, it is probably the conclusions from the 2010 SSRA that formed the uSSRA's basis for wearing N95 masks, but it is in contrast to the policy at FMD laboratories worldwide.

The committee also questions the data used to model the efficiency of N95 respirators. On p. 157, the uSSRA notes that a 2.5% failure rate for N95 respirators is expected because of a published failure rate (Cummings et al., 2007). The cited reference deals with poor N95 efficiency in workers in the aftermath of Hurricane Katrina, when the failure rate was actually around 75%, so the reference is not appropriate. The uSSRA also cites considerable N95 experimental penetration data (p. 100), and this may

be what allows it to use a 2.5% failure rate; however, these data are from studies that dealt with very controlled laboratory studies and did not take into account head movement, facial abnormalities, and other human (but non-fit) issues. Therefore, the committee views the use of a 2.5% failure rate in a real-life setting as an under-representation of reality.

Factors Related to Respiratory Transference

With respect to transference to the respiratory tract, the uSSRA assumes that failure rates due to poor fit of N95 masks would be only one-tenth the rate identified in a published study, in which failure rates of about 25% were found when the mask fit was poor. The uSSRA justifies the much lower rate based on the purported NBAF requirement that masks will fit correctly. Such a requirement may exist, but the basis for tenfold reduction seems poorly supported, especially because only a single study of mask failure is cited. It is not clear that human error is taken into account in this estimate of failure. The assumed failure rate seems overly optimistic, particularly in light of the physical exertion required of personnel working with large animals.

Although the wearing of N95 respirators may be a moot point, inasmuch as the change in SOP to require respirator use for FMDv work is not supported by literature, the committee is concerned that there are so many errors in the analysis of the data and the computations surrounding these respirators.

What Constitutes a System Failure

The uSSRA appears to assume 100% function or 0% function—all or none. It does not address functional disabilities that would adversely affect the efficiency of systems (such as incineration, autoclaves, EDS, and HEPA filtration) when it is less than 100% operational but has not indicated "failure." These may be subtle problems that do not appreciably affect sensors or monitors and thus would not detect partial loss of function. It is unlikely that all equipment and systems will operate at full 100% (perfect) function 100% of the time or that redundancy will always protect against such marginal failure conditions. It is also unlikely that systems that are not at 100% function will be at 0% function unless they are completely shut down. The question not addressed is how often systems would be less than 100% functional and how that would adversely affect, for example, efficiency of virus kill or reduction. Downtime for routine maintenance, repairs, and replacement when there is not likely to be redundancy was not addressed.

MODELING OF CATASTROPHIC NATURAL HAZARDS

The uSSRA attempts to model natural disasters caused by extreme winds (including tornadoes and hurricanes) and seismic activity. That was done to determine engineering requirements for ensuring the integrity of the biocontainment areas and to assess the risk of an envelope breach. The Manhattan, Kansas, site is in the heart of "Tornado Alley," and tornadoes are generally known as the most significant natural hazard threat for that area. Hurricanes and floods were discussed briefly but are not included as catastrophic events examined in the uSSRA. Earthquakes would not normally be considered a serious hazard in the area, but they are also assessed. It does not appear that the Riley County hazard and vulnerability assessment was reviewed as part of the uSSRA process; that could have informed the uSSRA on the highest risks perceived by those most familiar with the area.

TORNADOES

Tornado Risk Method

The uSSRA substantially extended and refined its treatment of tornadoes by transitioning from tornado F-Scale to Enhanced F-Scale (EF-Scale), using the leveraging method developed by the Pacific Northwest National Laboratory, including provision for the facility size and considering spatial variation of wind speed along the damage path of a tornado. A site-specific tornado risk model that relates tornadic wind speed with the annual probability of occurrence (or the mean recurrence interval, commonly referred to as the mean return period) is the most critical component of any tornado risk assessment study.

Tornado Modeling

The uSSRA provides an overall tornado risk analysis that is state of the art and that has been used by the Nuclear Regulatory Commission for power plant designs, and this analysis is an improvement over that provided in the 2010 SSRA. It uses an appropriate method, which includes additional data that are "event-based" rather than "segment-based"; the latter has inherent shortcomings. The uSSRA provides a continuous distribution of the strike probability of a tornado by wind speed and includes 5th and 95th percentiles. Due to insufficient sample size at higher wind speeds for large EF-Scale tornadoes, the estimated percentiles are influenced by this lack of data for high wind speeds which adds to the uncertainty for the estimates,

and the uSSRA noted that the estimates should be used with caution. The design wind speeds used in the uSSRA appear to be adequate for the design of such a facility with the prescribed probability of exceedance (POE).

Whereas the overall hazard analysis is state of the art, the results should have been analyzed by using more refined spatial techniques to observe tornado patterns, such as kernel density estimation (KDE). KDE is an interpolation scheme that emphasizes spatial patterns at a location rather than considering only locations where tornadoes were recorded. In light of the risks provided in the uSSRA, it is unlikely that any further refinement in analysis would yield changes that would affect the final cumulative risk across events.

Tornado Design Aspects

The uSSRA suggests that the current NBAF 65% designs provide a tornado-hardened zone to ensure protection against loss of containment in the event of a tornado and protection against envelope penetration and development of cracks up to wind speeds of 228 mph. The protection also includes defense against windborne missiles (such as projectiles and debris) that can become airborne in tornadoes and can result in serious damage.

Figures 2.4.5-2 and 4.6.3-3 of the uSSRA highlight the tornado-hardened sections of the NBAF to ensure the integrity of the containment and envelope. The uSSRA does not include any systematically derived fragility curve (e.g., conditional probability of failure or other adverse performance given the level of tornado loading) for each performance level to correspond with the established level of risk associated with tornado wind speeds. That would be necessary to demonstrate the efficacy of the designed performance levels of the containment system and its envelope. A fragility curve for a prescribed performance criterion would define a level of damage conditional on wind speed. When weighted with the corresponding probability density function of wind speed, it yields a probability of failure at the stated performance level. In the absence of a fragility analysis, it is assumed that no pathogens will be lost at the maximum design wind speed of 228 mph. The uSSRA also assumes that 100% of the MAR will be released if the winds reach 260–280 mph. That assumption is not backed up by a fragility analysis related to the integrity of the structural system or a breach of the containment. In the absence of a detailed catastrophic failure model for the NBAF, it has been further assumed that the releases between the design wind speed of 228 mph and the catastrophic wind speed of 260–289 mph follow a prescribed distribution. Those release levels should have been refined further with a fragility framework-based analysis, which would affect the annual probability of release due to tornado loading.

Assessment of Methods and Assumptions

The uSSRA does not include a systematically derived fragility analysis for different performance levels to correspond with the established level of risk associated with tornado wind speeds. In the absence of such information, it is not possible to assess the adequacy of the containment system performance under tornadic winds.

EARTHQUAKES

Seismic Risk Assessment

The uSSRA assesses the risk of earthquakes at the site by using U.S. Geological Survey spectral acceleration data to determine a 2% POE over 50 years at the NBAF site. Spectral acceleration is provided for two periods: 0.2 second and 1 second; these are appropriate starting points for the seismic analysis.

Those numbers are subsequently updated in the uSSRA with the NBAF design values. Rather than selecting a value of spectral acceleration commensurate with the dynamic features of the building's containment system—which would be a short period of ground shaking (for example, the 0.2-second hazard)—the uSSRA uses a 1-second value. Selecting a long rather than short event resulted in a POE over 50 years that is 20 times higher than what would be expected. Because the NBAF would be a low-rise structure, the uSSRA should have selected a short period of acceleration, which would result in a lower POE and lower hazard across events. It is important to note that the short period of ground shaking with lower POE also results in a higher degree of damage. It is not possible to know how it will affect the overall risk without conducting a systematic analysis of structural fragility; however, it appears that the uSSRA predicts cumulative risk across events that is excessively high.

Earthquake Design Aspects

In the uSSRA, it appears that the selection of earthquake ground acceleration and the associated performance of the structure at a given ground acceleration have been treated in isolation. The selection of ground motion in the uSSRA was used to assess the risk of pathogen escape as a result of cracks and breaches in the building envelope, whereas the seismic performance of the structure has been the responsibility of the architects and engineers at the NBAF Design Partnership. The lower ground acceleration associated with modeling a 1-second period would yield a higher POE, but would result in a lower level of impact on the structural response, would

result in lower level of cracking and ductile behavior, and may lead to a smaller probability of pathogen escape. It has also been stipulated that the NBAF Design Partnership would conform to the most current codes of practice in designing and constructing the facility.

The uSSRA anticipates that hardening the facility for tornadoes also improves the containment system's capacity to resist earthquakes and reduces the probable loss of containment caused by an earthquake. A performance-based multi-hazard analysis would allow complementary structural features to share load effects of different hazards. An integrated approach should have been used to appropriately account for hardened structural designs in assessing risk associated with multiple hazards (such as tornadoes and earthquakes).

A concern that arises with regard to the seismic analysis is the omission of the effect of vibrations on non-structural elements, including sensitive equipment necessary for filtering, ventilation, and control. To a large extent, this is a design issue and such lab appurtenances should be well secured and detuned from the main structure.

Assessment of Methods and Assumptions

The seismic risk analysis in the uSSRA fails to address fundamental issues in the selection of appropriate design spectral acceleration and the attendant performance of the containment system under design earthquake conditions. Therefore, the committee questions the estimated values of cumulative risk across events associated with seismic catastrophic events, and finds that the uSSRA overestimates the risk due to wind and seismic hazards.

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5

Evaluation of Fate and Transport Modeling

MODIFICATIONS IN USE OF THE MODEL AND PARAMETERS

The updated site-specific risk assessment (uSSRA) of the proposed National Bio- and Agro-Defense Facility (NBAF) has modified the dispersion modeling and analysis of the 2010 SSRA. It has responded to some of the previous criticisms by conducting sensitivity studies with the Second-order Closure Integrated Puff Model (SCIPUFF) to examine the effects of uncertainty in meteorological variables and model parameters on predicted doses; accounting for livestock distribution in computing the integrated dose (the dose is related to the risk of infection at any specified location relative to the release location); and using three different methods to estimate the risk of infection resulting from a dose of foot-and-mouth disease virus (FMDv).

The uSSRA uses SCIPUFF to estimate the exposure of a potential FMDv release from the NBAF and uses the North American Animal Disease Spread Model (NAADSM) to model airborne spread of FMDv once an infection is initiated. SCIPUFF is a Lagrangian air dispersion model that uses Gaussian puffs to model 3-D time-dependent dispersion of concentrations; it is available both in commercial and Environmental Protection Agency no-cost versions.

SHORTCOMINGS IN THE APPLICATION OF SCIPUFF

SCIPUFF is appropriate for modeling airborne transport and dispersion of potential releases from the NBAF, but the uSSRA's description of its application and the associated results are difficult to follow even for experts in

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transport modeling. The uSSRA used a meteorological classification scheme referred to as self-organizing maps (Kohonen, 1982) to generate meteorological inputs required to run SCIPUFF. Because this approach is generally not used in air pollution modeling, it is difficult to evaluate the validity of the claim that 95% of the meteorological conditions result in no infection. The graphics used to present the results convey little information. With such insufficient information, the committee found it impossible to evaluate the validity of the results.

SHORTCOMINGS IN MODELING AIRBORNE SPREAD IN THE NAADSM

The NAADSM is used "to simulate the spread and control of foreign animal diseases in a population of susceptible livestock herds" (www. naadsm.org). The NAADSM analysis includes a pathway to model the spread of infection through airborne transport of virus particles. The airborne spread model has two options to describe the probability of airborne spread of infection between two premises. The first option assumes that the probability of infection at a premise declines linearly with distance from the source of infection; this option was used in the 2010 SSRA. The second option assumes exponential decline with distance and is used in the uSSRA (p. 440); exponential decline is further explained in the NAADSM user's guide. The linear model typically leads to lower probabilities of spread over shorter distances and higher probabilities over longer distances.

The uSSRA states that the adoption of the exponential option was based on FMDv dispersion modeling results as illustrated in Figure 6.1.4-19 (p. 442). However, the uSSRA does not show how these results are derived from the results presented in the cited references (Garner and Cannon, 1995; Sørensen et al., 2000) or those from SCIPUFF as described in Volume I of the uSSRA. Furthermore, it is unclear how these results were used to specify the parameters of the airborne spread equation on p. 67 of the NAADSM user's guide.

Figure 6.1.4-19 of the uSSRA indicates that the uptake of plaque-forming units by cattle falls off by an order of magnitude when the distance increases by a factor of 2.5 from 2 to 5 km. That result is inconsistent with the statement made in the uSSRA that according to Garner and Cannon (1995) the risk of infection is expected to fall off linearly with distance under stable atmospheric conditions. It might be more appropriate to assume that the risk of infection is inversely proportional to the distance from the source because the risk of FMDv exposure is high when the atmospheric boundary layer is stable (Garner and Cannon, 1995). Under these conditions, the shallow boundary layer limits vertical dispersion, and the growth

of horizontal plume spread is at most linear with distance from the source (Venkatram and Wyngaard, 1988).

The uncertainty in the NAADSM airborne spread model suggests the need to conduct sensitivity analyses to examine the effects of both model formulation and parameter values on FMDv spread and hence on the economic impact of FMDv release from the NBAF. A sensitivity analysis should have been included in the uSSRA, as it would also indicate the role of airborne spread relative to other modes of spread.

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6

Evaluation of Epidemic Modeling

The use of computational models for epidemic forecasting is challenging. Epidemic models are constructed by narrowing down broad scientific understandings to specific parameter estimates and assumptions. Gaps in scientific knowledge, limitations on data-collection resources, and the complexity of the transmission processes themselves all make it impossible to precisely predict the consequences of an infectious disease outbreak. The very process of model construction requires simplifying assumptions that introduce more uncertainty. The use of models to inform disease control policies in the face of animal disease epidemics has been the subject of considerable debate (Anonymous, 2001; Kitching et al., 2005, 2006; Dickey et al., 2008; Mansley et al., 2011; Smith, 2011). Kitching et al. (2005, 2006) and Mansley et al. (2011) comment that the misapplication of foot-and-mouth disease (FMD) epidemic forecasting can be misleading and can promote a false sense of security. Forecasts in most fields of natural sciences are best viewed skeptically. Despite the limitations, epidemic modeling can be a useful conceptual resource because it forces a systematic review of all components of an infectious disease outbreak, including critical assessment of knowledge and uncertainty about each component.

OVERVIEW OF METHODS AND ANALYSIS

Section 6 of the updated site-specific risk assessment (uSSRA) estimates the consequences of a potential release of FMD virus (FMDv) from the proposed National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas. As in the 2010 site-specific risk assessment (SSRA), the uSSRA uses

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the North American Animal Disease Spread Model (NAADSM) in conjunction with data, statistical methods, and references from scientific literature. Simulation outputs from NAADSM were used to evaluate the impact of FMD spread through Kansas and into six adjoining states in different release events. The analysis estimated the consequences of large epidemics and the potential effects of some mitigation measures on an epidemic. Depending on the risk scenarios, the outputs suggested that an epidemic in the seven states could last 18 months or more and result in the loss of tens of millions of animals. The 2010 SSRA results were criticized by the previous National Research Council committee for a lack of transparency, structural limitations in NAADSM, and some specific modeling choices (NRC, 2010). The uSSRA makes a variety of changes and attempts to address all the previously identified shortcomings of the 2010 SSRA. The revised model in the uSSRA now estimates an FMD epidemic in these seven states to last about twice as long as and affect several times more animals than the 2010 SSRA.

SUMMARY ASSESSMENT

The overall methodology and presentation of epidemic modeling in the uSSRA are substantially improved compared to those in the 2010 SSRA. Part of the reason is the uSSRA's better description of model limitations and uncertainty. Issues of reliability, uncertainty, and sensitivity are acknowledged at the beginning of Section 6 of the uSSRA and addressed again throughout. The breadth of epidemiological material collected in the uSSRA could make it a useful reference for future FMD research and planning.

However, the epidemic modeling in the uSSRA still provides only a limited picture of the likely possibilities involved in an FMD epidemic originating in Manhattan, Kansas. Some of the limitations result from inadequacy of available tools, including NAADSM, some from lack of data and incomplete scientific understandings, and some from incomplete characterization of the resources and capacity for mitigation responses. Practical considerations have imposed a number of those limitations, as the uSSRA acknowledges. The committee finds that the modeling results underestimate the absolute size and duration of epidemics, in part because of a number of specific assumptions used in the uSSRA. Overly optimistic assumptions were made about response resources and capacities anticipated to be available by 2020, and these in turn would lead to an underestimation of the magnitude, duration, and economic impact of an FMDv escape from the NBAF in Manhattan, Kansas. The uSSRA underestimated contact risks and used overly optimistic parameter values for diagnostic capabilities, surveillance, contact rates, vaccination, and response. Consequently, the uSSRA spread model results incorrectly indicate foreshortened spread and low impact estimates. The incomplete data on interstate direct contacts,

including illicit livestock movements and interstate indirect contacts (fomites), would inhibit simulated movement, including secondary and tertiary spread of virus and infected animals from Kansas to the six other states.

Considering the aggregate of design, methods, data, and assumptions, the committee finds that the methodology as a whole lacks the overall validity necessary to predict with reasonable confidence the outcome of an FMD epidemic emanating from an FMDv release from the NBAF in Manhattan, Kansas. Much of the lack of validity was unavoidable, due in large part to many ill-defined or unknown factors. These factors lead to considerable uncertainty stemming from an absence of quality data and the vagaries of proposed mitigation policies on the outcome of an FMD outbreak. It is also important to note that these limitations may well lead to underestimates or misestimates of the consequences of an epidemic, which are carried over into the economic analysis. However, the committee strongly agrees with the uSSRA's broad conclusion that negative consequences of an FMD epidemic originating in Manhattan, Kansas, will probably be severe. The committee therefore agrees that great emphasis needs to be placed on preventing release of FMDv and detecting and containing FMDv if it escapes.

METHODOLOGICAL LIMITATIONS

Limitations of the Scope of Model

The committee noted two major shortcomings related to the geographical and outcome scopes. First, the spread model incorporated only seven states. According to the uSSRA, no suitable model for nationwide FMD prediction is yet available. Thus, absolute impacts reported in the uSSRA are acknowledged to be underestimates. The committee concurs that extension of the assessment to include spread through the contiguous United States, Mexico, and Canada would require several-fold greater effort (GAO, 2002). Second, there was no scenario involving FMD becoming endemic. Endemic FMD would require different long-term control strategies, such as a vaccination-to-live strategy, extensive laboratory testing for surveillance, and an expensive long-term eradication program.

Limitations of NAADSM

Like all models, NAADSM provides an imperfect representation of FMD spread and control and is based on a variety of simplified assumptions. As pointed out repeatedly in the uSSRA, use of only NAADSM, without application of support models, carries a number of structural limitations that force many ad hoc approximations to transmission and mitigation processes, resulting in a significant decrease in the reliability

of simulation results under at least a subset of important conditions. The limitations include the following:

- NAADSM can describe only regional transmission, in this case, within a single state; it cannot account for bidirectional transmission across state borders.
- NAADSM cannot address infection in wildlife, including feral swine populations.
- NAADSM is not designed to include facilities that house multiple animal species.
- The spread submodels between facilities make artificial assumptions about movement mechanisms and do not allow for accurate representation of livestock movement patterns.
- There are no means of representing zoned movement controls in response to an outbreak.
- The current implementation does not allow realistic modeling of the livestock culling process, inasmuch as NAADSM cannot adequately account for handling times and logistic limitations (p. 451 of the uSSRA). Nor does NAADSM allow options other than culling for the final disposition of herds that are immune after infection (p. 478 of the uSSRA).
- The current implementation does not allow realistic modeling of the distribution and use of vaccines during an outbreak; it does not allow for simultaneous administration of vaccines directly by producers, and it assumes an unlimited vaccine supply (p. 456 of the uSSRA).
- NAADSM allows users enormous latitude in defining the qualitative and quantitative components of transmission. This is one of the strengths of NAADSM and also its major weakness, as it relies on expert opinion to define components. Model outcomes are very sensitive to parameter assumptions, and even when expert opinions are used they can vary and lead to wide probability distributions (Bates et al., 2003).

The uSSRA discusses those limitations and the ad hoc approximations that they necessitated. Whereas these approximations likely prevent development of accurate and nuanced understandings of the consequences of variation in the logistics of mitigation, they serve as reasonable placeholders for the broad-brush results obtained in the uSSRA. Resolving these limitations will eventually require redesign of NAADSM or a switch to a more flexible simulation platform.

Limitations of Available Data

The uSSRA also points out many limitations in the data available for use in NAADSM modeling, which add to the uncertainty of the results presented. The limitations in the data include the following:

- The relationship between dose of FMDv and probability of an infection of an individual animal in large (e.g., thousands of animals) and in small (e.g., less than 100 animals) herds was not clarified. The relationship is expected to vary, depending on FMDv serotype and strain, animal species, and route of exposure, as well as on the size of the herd.
- Potential exposure of Kansas State University faculty, staff, and students; NBAF employees; and Foreign Animal Disease Diagnostic School participants to livestock.
- Distributions and movements of feral swine and of susceptible wildlife, such as elk and deer that may have potential for transmitting FMDv to livestock (Rhyan et al., 2008; Moniwa et al., 2012).
- Animal movement (direct contact) and fomite movement (indirect contact) within and among states in the region modeled and long-range movement of susceptible animals from the region to other states.
- Data on producers who are noncompliant with state and federal regulations regarding veterinary inspection, animal identification, and permitting and documentation of animal movement for those who buy and sell through informal arrangements and who contribute to disease spread through comingling of livestock at non-regulated events (such as swap meets) or illegal animal movements.
- Some data sources used in setting model parameters are not publicly available, which obstructs transparency and hinders independent replication of the uSSRA's results.
- Although the uSSRA's livestock database created for the Manhattan area is a strong data contribution for a snapshot in time, such data can become quickly outdated with changing numbers of animals, species, and livestock movements. The uSSRA did not reference any state or federal documents that would describe a mechanism for accurately identifying and updating active premises. In the face of an FMD outbreak, it will be critical to already have in place well-validated state animal health databases, active surveillance, and premises identification.

Dose–Response Modeling and Minimum Infectious Dose

The uSSRA uses probit analysis to estimate the population probability of infection associated with low doses of FMDv; the risk depends on the probability of exposure to at least one viable virion when index cases are

simulated. Probit analyses can provide appropriate low-dose risk estimation for some pathogens, but the committee has concerns about the development and use of probit analyses for FMDv in the uSSRA.

First, use of the probit model instead of other dose–response models merits more examination and justification than was included in the uSSRA. The [log-]probit model can in some cases underestimate dose–response (Gale, 2001) compared with the estimates produced with the exponential or beta-Poisson models. The committee is aware that uSSRA Appendix Section A6.1.2.1 states (p. A6-7) that "the exponential and beta-poisson [sic] model were also considered; however, the potential of these models to characterize the dose-response relationship of FMDv in cattle and sheep was previously studied by French et al. and was found to be unsatisfactory, particularly at low doses." The cited dose–response modeling from French et al. (2002), however, is at odds with the text in the uSSRA, and the uSSRA does not adequately consider the French et al. analyses or earlier work by others (Sutmoller and Vose, 1997; Cannon and Garner, 1999) that were cited by French et al. (2002). The uSSRA should have provided a more accurate and transparent analysis of the cited literature and provided further details to compare results of an exponential analysis with those of a probit analysis.

Second, it appears that relevant data from experimental studies were excluded, and their omission may limit the range of data used in the probit estimates. Specifically, the excluded data were related to animals that seroconverted but did not show evidence of shedding in the once-daily sampling schemes. Those animals could be the very ones that should be included in the probit analysis. The animals had become infected by virtue of the seroconversion, perhaps by a low dose that resulted in short-duration shedding that was not detected in 12-hour or 24-hour sampling intervals. Inclusion may have improved the probit-derived probability estimates of low-dose infectivity.

Third, the committee is concerned about continued use of the "minimum infectious dose" (MID) concept. The uSSRA states on p. 408 that

> Many researchers have proposed that there is no risk of infection for doses of FMDv lower than a certain amount, called the 'minimum infectious dose'.... These values might represent a phenomenon in which a minimum number of pathogen particles are required to overcome host defenses and establish an infection, or they could be an artifact of the use of a small number of animals in infection experiments (i.e., if five animals were used, identifying doses that cause less than a 20% probability of infection is difficult).

The latter argument is legitimate in that these experiments have sample sizes that are statistically inadequate to estimate the risk of infection at low doses (Haas et al., 1999; NRC, 2005). However, the "minimum infectious

dose" concept is not credible. The comment about researchers proposing no risk below a particular threshold is related mainly to the older microbial risk-related literature. Recent work (e.g., Haas et al. 1999; Gale, 2001) typically applies dose–response modeling with the best available data (possibly including meta-analyses) and extrapolates low-dose with probit, beta-Poisson, exponential, or other dose–response models. For pathogens on which reliable data for dose–response analyses are available, there is no population threshold dose (NRC, 2005).

Fourth, the uSSRA does not provide an adequate discussion of the uncertainties in the FMDv dose–response modeling using the probit model or its alternatives nor does it provide an adequate discussion of their application to predicting herd response. Failure to do so may leave the impression that the dose–response predictions used in the probit model are highly certain, and this is not the case. The statistical reliability of dose–response modeling is briefly discussed, but its impact on the results is not adequately analyzed. Results could be sensitive to uncertainties such as FMDv strain differences, experimental dosing regimen (often bolus) compared to the potential herd exposures resulting from a leak, and differences between the experimental animals' status and that of the target animal herds (e.g., species or breed, immune competency, concurrent infections, environmental stresses). The direction and magnitude of these effects may be unknown for FMDv, but they nevertheless remain as uncertainties in the extrapolation to herd response that were not adequately addressed in the uSSRA.

Assumptions About Available Response Resources and Capacities

The uSSRA makes various assumptions about foreign animal and zoonotic disease response capabilities presumed to be in place at the time of the anticipated NBAF opening in 2020. It will be important to have these tested capabilities in place from day 1 to mitigate the effects of an accidental release of an infectious agent. The committee notes that many of these assumptions are unrealistic today and that making them realistic would require major investments and considerable political will before the NBAF opens. Whereas the uSSRA does not discuss future investment requirements, it does acknowledge that capabilities will be changing over the next 8 years. Concerns about the assumptions related to capabilities include the following:

- Vaccination would begin very early (on day 7) in an FMD epidemic. Also, once vaccination is initiated, single-dose, high-potency, 100% efficacious emergency vaccine would be available in unlimited quantities. It is further assumed that 100% of vaccinated animals would be protected from infection. These assumptions would apply for all 7 serotypes of

FMDv and for all the strains within each serotype that could escape from the NBAF. These assumptions are inconsistent with the current state of knowledge.

- It would take 3–11 days to vaccinate all herds in Kansas (an average of 90 herds per day).
- 100% of cattle and swine producers will report a suspicious case in less than 2 weeks following infection; this is unrealistic.
- Laboratory testing capacity for the presence of FMD virus (RRT-PCR [Callahan et al., 2002]) and virus isolation and for the presence of antibody is assumed to be unlimited, with a range in the turnaround time for testing of only 0–2 days. Laboratories in the National Animal Health Laboratory Network currently do not have the capability to conduct serological tests for FMD.
- Diagnostic laboratory tests are assumed to be of exceptionally high accuracy and reliability, and perfect accuracy is assumed in detecting FMD on 100% of infected premises.

Furthermore, the lack of real-time FMD surveillance, as acknowledged in the uSSRA, diminishes the likelihood of early detection and control.

The uSSRA states that "economic estimates based on the outputs of the economic model for the Updated SSRA will, again, underestimate the absolute impact of the outbreak of FMD originating from the NBAF because the outbreak is artificially limited to the region modeled instead of the whole of North America" (p. 405). Many of the limitations listed above are also likely to result in underestimation of the extent and cost of a potential release of FMDv from the NBAF in Manhattan, Kansas.

Other Sensitivity Analysis

The epidemic modeling section provides the only sensitivity analysis that has any degree of rigor in the three volumes of the uSSRA. This section of the uSSRA provides a correct and important caveat about the usefulness of the estimates (p. 534):

> This analysis informs how much confidence can be placed in the results as absolute reflections of the impact of an FMD outbreak given that some of the modeling parameters are based on scanty evidence. As discussed, epidemiological models are best used to understand relative risk and relative benefit of risk mitigation measures because inaccuracies in a model are reflected in the baseline and experimental cases, largely cancelling each other out.

The uSSRA further discusses that variation in the contact rate of less than an order of magnitude (a factor of 0.5–2) changes the duration of an

epidemic by over an order of magnitude (see pp. 537–538). However, many parameter values have greater uncertainty—with ranges that span several orders of magnitude. Distributions based on these wider ranges should have been provided in the sensitivity analyses because that would provide better information on the most important components of uncertainty in the results.

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7

Evaluation of Economic Modeling

OVERVIEW OF METHODS AND ANALYSIS

The economic analysis in the updated site-specific risk assessment (uSSRA) of the proposed National Bio- and Agro-Defense Facility (NBAF) is more comprehensive than other economic analyses of foot-and-mouth disease (FMD) outbreaks (Ekboir, 1999; Paarlberg et al., 2002, 2008; Pendell et al., 2007; Hagerman et al., 2012). The uSSRA relies on three components to predict the economic consequences of an FMD epidemic: a partial equilibrium model, a regional model, and accounting of government non-indemnification costs. A partial equilibrium model of the U.S. agricultural sector describes supply and demand for U.S. livestock products, livestock, and major feed crops in global markets. A regional model captures the changes in expenditure in the 7-state region surrounding the NBAF. The models determine the impact of depopulating livestock during an outbreak, of reductions in U.S. consumer demand for livestock products, and of reduced exports of livestock products on market prices, quantities, economic welfare, and expenditure. The change in economic welfare is determined by adding the changes in returns to producer capital and management, consumer surplus, indemnification costs, changes in regional non-agricultural expenditure, and government non-indemnification costs, including surveillance, destruction, and mitigation. Compared with the 2010 SSRA, the updated analysis relies on an updated baseline with solutions for 40 quarters versus 20 quarters. Revisions in the epidemic modeling that extend the magnitude and duration of an outbreak are captured in revisions of the economic results. The uSSRA's use of a dynamic equilibrium model and a

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regional model are appropriate, but the committee has concerns about the analysis for reasons noted below.

INACCURATE DESCRIPTIONS OF METHODS AND ANALYSIS

Descriptions of the model and scenarios in the uSSRA are sometimes inaccurate. The partial equilibrium model is described as temporal and spatial; the latter is inaccurate. The model is temporal in that it solves dynamically to capture the lags inherent in animal and crop production. The model is not spatial inasmuch as it treats the United States as a point in space, so the uSSRA text incorrectly implies that the model handles regional differences in production and consumption and hence regional trade, which the model is not capable of handling.

The uSSRA also states that observed values are used for the 2009–2018 model baseline (p. 546), but observed values are only possible for 2009 and 2010 and not future timeframes. For 2011–2018, the model baseline is the annual U.S. Department of Agriculture (USDA) baseline from February 2011 converted into quarterly values. That means that there is more fluctuation in the 2009 and 2010 results because the USDA baseline tends to smooth out. The FMD supply shocks are introduced into the more variable baseline values. The inclusion of farm programs based on the 1996 and 2002 farm bills is mentioned on p. 545 of the uSSRA, but this version of the model incorporates the 2008 farm bill and the Average Crop Revenue Election (ACRE) program. Given the baseline crop prices, the only change in government payments to crop producers is via ACRE unless reduced feed consumption causes crop prices to fall enough to trigger traditional commodity program payments. Thus, the timeframe of 2009–2018 matters for the results because changes in U.S. government payments will not buffer losses in returns to crop growers except for the small share of production enrolled in ACRE.

In the uSSRA, there is a tendency for the text to refer to cattle, and this leaves the situation for other species vague. For example, it is unclear whether the vaccinate-to-live strategy applies to swine and sheep as well as to cattle. The uSSRA should have described the domestic demand shocks as percentage reductions in domestic demand rather than as consumers dropping meat consumption, because consumers could reduce consumption without completely avoiding red meats.

INSUFFICIENT INFORMATION PROVIDED TO VERIFY RESULTS

The quality of the estimates of economic impacts depends on input from the North American Animal Disease Spread Model, correct operation of the economic models, and decisions on scenario design. The magnitudes of livestock depopulation are estimated in the epidemic modeling. Those

values are converted into supply reductions and combined with demand shocks, including U.S. domestic consumer behavior and export reductions. The text and tables in the uSSRA are insufficient for the reader to replicate and evaluate the economic results.

At times, the discussion in the uSSRA does not correspond with information provided in the tables. The discussion of how supply shocks are estimated is confusing, and the information in the tables cannot be used to determine whether the supply shocks are implemented correctly. A more detailed table to illustrate the magnitudes of supply reductions for a multi-quarter outbreak would have been useful. The demand shocks as described in the text and as reported in Table 7.3.1-9 appear to be in conflict, probably because of the wording of column headings (p. 563 of the uSSRA). The text indicates that domestic demand begins to recover in the quarters immediately after the end of an outbreak, but the table shows 10% demand reductions in the p50/p50 case for the end of the outbreak + four quarters with recovery beginning in the 5th quarter after the outbreak ends.

PARTIAL EQUILIBRIUM MODEL ANALYSIS

The partial equilibrium model includes livestock products, animals, and major crops at a national level. In response to supply disruptions and reductions in domestic and export demands, the partial equilibrium model determines the quarterly time path of changes in market prices, quantities, and measures of economic welfare. Government indemnification, surveillance, mitigation, and control costs are also calculated. The uSSRA uses the partial equilibrium model, and this is a proper approach. The validity of the analysis depends on the quality and validity of the economic shocks and how the model is used. The committee finds that the upper ranges for the supply shocks, the outbreak duration, and other aspects of scenario design, which were derived from the epidemic modeling, are underestimated. The committee therefore concludes that the magnitudes of the estimated economic impacts are also underestimated.

In responding to an FMD outbreak, the vaccinate-to-live decision for outbreaks consisting of 180 days or more is important for the results. Vaccinated animals remain in the supply chain, and knowledge that vaccinated animals are in the meat supply could affect consumer response. The text is unclear about how vaccinate-to-live is reflected in the modeling: it is unclear whether those animals are excluded from the supply shocks. If so, it is unclear whether the supply shocks go to zero for quarters 3 and beyond or whether animals are still waiting destruction; the latter could affect continued supply reductions. The text does not explain that the greater assumed demand reductions for longer outbreaks partly incorporate a consumer response to having vaccinated animals in the supply chain.

The change in producer welfare is described as producer surplus, but it

is actually the return to capital and management. Although they are similar concepts, there are slight differences in these measures. In the partial equilibrium model, crop producers are separated from land owners, so all crop producers are modeled as tenants to isolate the changes in land rent. The change in returns to land owners should have been included in the reported uSSRA results.

REGIONAL MODEL ANALYSIS

Regional modeling determines non-agricultural changes in economic activity in the 7 states experiencing an outbreak. The regional analysis is an important component because it captures economic impacts on sectors within the 7-state region that are excluded from the partial equilibrium model. Although the regional non-agricultural costs are not large—$40 million to $6 billion in the context of the total economic impact of $16–140 billion—it is important to include such costs. These costs are concentrated in a 7-state region and concentrated on a small set of industries within that region. Because the regional model and modeling approach differ from the partial equilibrium model, care must be exercised when using these in the same analysis. The Regional Input-Output Modeling System (RIMS II) developed by the Bureau of Economic Analysis is well known and has been available for some time. Although there is extensive discussion of the regional model in general, decisions were made about multipliers (such as regional aggregation and leakages), and the multipliers used in the regional model were not included in the uSSRA but are necessary for evaluating the regional results.

Table 7.3.2-2 of the uSSRA reports expenditures for travel by state. The effect of an outbreak on travel is a major component of the regional analysis. The use of changes in expenditure as a measure of regional non-agricultural welfare effects as suggested by the table on p. 568 is a concern. A change in expenditure is not a measure of a change in economic welfare unless utility is held constant. But Table 7.4.1-1 of the uSSRA shows that changes in regional non-agricultural expenditure are added to the changes in producer returns to capital and management, consumer surplus, indemnification, and government non-indemnification costs to give the change in total economic welfare. The change in expenditure is correctly described in the text as the change in economic activity. Changes in expenditure exceed changes in economic welfare because the change in expenditure does not account for adjustment in variable costs. An alternative closer to theoretically correct measures of economic welfare—such as the return to non-traded, quasi-fixed inputs (value-added)—would have been a better choice if available.

NON-INDEMNIFICATION COSTS

The values for government costs used in the 2010 SSRA are adjusted for inflation and are used to determine government non-indemnification costs. There is extensive reporting of depopulation and vaccination costs in Section 6, but it is not clear why that information is not used to model economic impact in Section 7 of the uSSRA. Government costs that would have been incurred regardless should be excluded, and only additional costs incurred by government should be included; otherwise, the estimated government non-indemnification costs that are reported are higher than the actual additional costs incurred.

SUMMARY

The economic modeling approaches used in the uSSRA are frameworks that, if used properly, can address the economic impacts of an FMD outbreak that results from a breach of containment at the NBAF. The uSSRA attempts a more comprehensive analysis than existing analyses. Nevertheless, there remain concerns about the uSSRA. The information provided in the text and tables is insufficient to determine whether the analysis was done correctly. There are concerns about aggregating the results of differing modeling approaches into an aggregate economic impact. The economic consequences are generated from results obtained in the epidemic modeling. The committee believes those depopulation and duration estimates are underestimated, and consequently the supply reductions and the demand reductions used as inputs into the economic analysis are also underestimated.

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8

Evaluation of Biosafety Level 4 Assessment

The 2010 site-specific risk assessment (SSRA) of the proposed National Bio- and Agro-Defense Facility (NBAF) did not adequately address the unique issues and challenges associated with work in a maximum-biocontainment environment, and the previous National Research Council committee was therefore led to conclude that the 2010 SSRA did not adequately characterize risks associated with biosafety level 4 (BSL-4) containment activities. An overall risk assessment of the NBAF BSL-4 would need to include an evaluation of the *additive* risks posed by all BSL-4 work, including the risk of a release from the BSL-4 associated with use of large animals in the BSL-4 suite, the risk of a release associated with non-animal-related activities in the BSL-4 suite, and the risk of a release from the BSL-4 suite associated with natural disasters. The epidemiological and economic impacts of such a release would then need to be evaluated as part of the risk assessment. The committee recognizes the inherent limitations in the available information regarding henipaviruses (see below) that formed the basis of the BSL-4 review and regarding other agents that may be studied in the BSL-4 suite. However, the risk assessment presented focuses on only one component of the overall risk, namely, the *unique* risks of release from the BSL-4 suite associated with the use of large animals. During the March 2012 meeting of the present committee, the Department of Homeland Security (DHS) indicated that it assessed only BSL-4 risks associated with large animals on the basis of its interpretation of the previous committee's evaluation, which was misunderstood. The uSSRA does not consider the overall risk and presents a limited qualitative assessment, and therefore the evaluation likely underestimates overall risk related to the BSL-4 suite.

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INADEQUACY OF THE SEMI-QUANTITATIVE APPROACH

The uSSRA responded to the congressional mandate by conducting a semi-quantitative risk assessment on the only two exclusively BSL-4 agents that are on the priority list for work at the NBAF: Hendra virus (HeV) and Nipah virus (NiV). HeV and NiV are paramyxoviruses (*Henipavirus* genus) that were recognized in the 1990s and produce high-mortality disease in animals and humans (Eaton et al., 2006; Field et al., 2007).

The uSSRA states that the primary objective of the BSL-4 risk assessment is "to identify and characterize the unique risks associated with working with large animals in BSL-4 conditions." The analysis therefore focuses exclusively on risks associated with handling infected large animals in BSL-4 containment. The uSSRA modeled four potential release pathways (aerosol, solid, liquid, and transference) and developed scenarios in consultation with an international panel of experts in high-containment settings and pathogens (including representatives of the Australian Animal Health Laboratory in Geelong and the Canadian Science Centre for Human and Animal Health in Winnipeg). The committee commends DHS for consulting an international expert panel to delineate the major and unique risks of the BSL-4 environment.

Some risks are inherent to working in a BSL-4 environment, which include the use or manipulation of dangerous pathogens that are highly lethal to humans or animals and for which there are no preventive or therapeutic interventions. Added to those risks are the combination of the presence of large animals in the maximum-containment environment coupled to the difficulty of maneuvering in biocontainment suits and with separate air supplies. These difficulties raise the risk of injuries, disruptions in air supply, and compromised suit integrity from holding pens, animal bites, inoculations, and use of sharp implements during experiments and necropsies. These hazards highlight the importance of having administrative measures in place—including buddy requirements for BSL-4 systems—to ensure recognition and reporting of such breaches and occupational health programs to ensure proper management of personnel.

CONCERNS ABOUT BSL-4 ANALYSIS

The committee concurs with the finding in the uSSRA that transference represents the major risk of inadvertent escape for BSL-4 pathogens relative to other release pathways. However, the committee has many concerns about the analysis and found that the uSSRA does not adequately address the overall risks related to work with BSL-4 pathogens; it elaborates on those below.

Lack of Consideration for Full Array of BSL-4 Activities

The uSSRA focuses exclusively on risks associated with handling of large animals in BSL-4 containment and neglects risks posed by other activities in BSL-4 containment. Work in a BSL-4 laboratory that does not house large animals is not risk-free as implied by the uSSRA. Due to the nature of BSL-4 pathogens, work that would normally be conducted in BSL-3 special procedure or BSL-3 Enhanced areas of the facility are required to be conducted in BSL-4 if it involves live virus. The 20-year record for safe operation of major BSL-4 laboratories in the United States is excellent (Johnson, 2003) and the use of biosafety cabinets and other biosafety measures in the BSL-4 laboratory setting can reduce the risk of release from non-animal-related activities, but it does not reduce the risk to zero. Consequently, by omitting the risk of activities in non-large-animal BSL-4 space, the uSSRA does not address "overall risks" as this committee had expected because it ignores these risks.

Magnitude of Risks Associated with Unknown or Uncharacterized Pathogens

The uSSRA notes that NiV and HeV are not the only pathogens that would be examined in the BSL-4 laboratory. As part of its mission to serve as a world-class laboratory, the NBAF is expected to conduct essential and cutting-edge research both on known BSL-4 agents and on unknown and uncharacterized pathogens. There is a possibility that experiments would involve large animals for hemorrhagic fever agents, variant influenza viruses, or pox viruses, and work on these pathogens will pose risks. As the microbiological and epidemiological features of these agents differ from those of henipaviruses, it is likely the risks associated with working on these agents would also be different from those of henipaviruses. The committee concurs that it is difficult, if not impossible, to model the risks associated with unknown agents. However, the uSSRA provides only a minimal risk estimate, and the present committee echoes the previous committee's concern that the risk assessment did not adequately discuss "the magnitude of risk and the strategy or process flow to identify and mitigate risk in future research areas" (NRC, 2010, p. 94).

Scenarios Not Fully Developed or Characterized

The uSSRA modeled 109 scenarios in the BSL-4 assessment, but the risks associated with some of them were not fully developed. For example, the necropsy scenario does not consider what the procedure entails with regard to livestock, including the use of knives, saws, rib cutters, and various

other surgical instruments for collecting fluids and tissues. Those activities pose among the highest risks of exposures in the BSL-4 laboratory, but these events are covered in only a single scenario in the uSSRA.

Failure to Consider Natural Disasters

For FMDv, the risk analysis includes potential releases associated with tornadoes and earthquakes. The uSSRA concludes that the overall risk of release for FMDv, although low, is higher for these natural disasters than for any non-disaster scenarios. Although the relative risks in the BSL-4 environment are likely to differ because of the potential for escape via human infection (transference), if one accepts the contention that natural hazards create the greatest risk of releases from the BSL-3 laboratories, the risks associated with natural disasters are also likely to be higher for the BSL-4 laboratories than those associated with the other pathways modeled in the risk assessment. The potential for natural disasters to affect the BSL-4 portions of the facility is not mentioned in the assessment of BSL-4 risks, and the committee wonders why the uSSRA fails to consider natural disasters as part of the BSL-4 risk assessment. Although the facility would be designed to withstand many natural disasters, there is a potential for loss of containment because of pressure fluctuations that can occur during a tornado or loss of structural integrity during an earthquake; this constitutes a significant omission and leads to an understatement of the risks associated with the BSL-4 containment suite.

CONCERNS ABOUT USE OF METHODS AND MODELS

Because the BSL-4 semi-quantitative assessment used an approach similar to the epidemic modeling of foot-and-mouth disease virus (FMDv), the modeling concerns expressed in Chapter 6 of the present report regarding the assessment of FMDv also pertain to the BSL-4 assessment. For example, the uSSRA calculated probabilities as the simple product of individual risks, which fails to recognize the potential interdependence of risks; for example, a single mechanism of failure may simultaneously impact multiple nodes, meaning these nodes are not completely independent and cannot be illustrated as a simple product. In addition, the uSSRA treats all mechanical errors and human errors as equivalent by using a single numeric value for each in all the risk calculations in the BSL-4 section of the uSSRA. Taken together, these factors may have artificially lowered the calculated risk probabilities.

Inappropriate Extrapolation of Data and Assumptions

The committee recognizes that limited data are available on NiV and HeV and that no studies have been performed for some of those data gaps. The uSSRA attempts a semi-quantitative approach, which would be commendable; however, some assumptions and extrapolations are inappropriate, including the calculations of infectious dose and relative impact.

The calculation of infectious dose (which is a critical factor in this modeling) uses data based on intraperitoneal injections into Syrian hamsters to estimate infectious dose in large animals and humans. The uSSRA extrapolates the infectious dose in large animals and humans on the basis of weight. Allometric scaling is used in chemical risk assessment but is not an accepted practice in microbial risk assessment, in which the initial inoculum can replicate. The extrapolation fails to recognize that the infectious dose–response curve may not be linear. In addition, the uSSRA uses lethal dose (LD_{50}) instead of an infectious dose–response analysis because of unavailability of data on which to model the latter. The committee recognizes that because these agents are associated with high mortality, the LD_{50} may not vary substantially from the infectious dose, but the use of LD_{50} is likely to cause artificially high estimates of the dose necessary to produce infection in humans and large animals. As a result, the threshold Q values included in Table 9.9.2-2 of the uSSRA appear to be speculative at best and are probably inappropriate.

The current practice in microbial risk assessment uses dose–response modeling when data are available, as opposed to the minimum infectious dose (MID) approach used in the uSSRA. As previously mentioned in Chapter 6 (see the section "Dose-Response Modeling and Minimum Infectious Dose"), the committee finds the use of MID to be unacceptable. Data-driven dose–response modeling (including model selection via goodness-of-fit testing) may be limited by the availability of suitable data, but a discussion of uncertainty would cover the accepted one-hit (no-threshold) concept (NRC, 2005) with extrapolation at very low doses for infectious dose–response.

The relative impact section (Section 9.9.2.2 of the uSSRA) uses data from the 30 recognized outbreaks of HeV in Australia and the 14 recognized NiV outbreaks in Malaysia, Bangladesh, and India. The uSSRA acknowledges that conditions in those locations are substantially different from conditions in Kansas, especially animal husbandry practices and the availability and quality of human health care. However, the committee is perplexed that the uSSRA would use the mean value to make calculations, such as the number of animals affected in a possible release and the number of human illnesses. For NiV, the initial outbreak in Malaysia resulted in the culling of more than a million pigs, whereas none were culled in any

of the other outbreaks, because these outbreaks occurred in settings where pigs were not present and were due to different modes of transmission. The uSSRA uses an average number of 71,400 animals per outbreak in subsequent calculations, which disregards the statistical principle of excluding outliers. Similarly, the uSSRA uses a value of 0.23 humans affected per outbreak of HeV (the average of 7 human cases in 30 outbreaks). The committee finds that these values are not soundly derived and thus not valid.

Given these significant limitations, the calculations in the more quantitative sections of the BSL-4 assessment seem highly speculative. And the committee reaches this conclusion without even further addressing the limited epidemiological and economic information that was included in the uSSRA relative to BSL-4 pathogens.

Wildlife Reservoirs

In assessing the potential consequences of a BSL-4 pathogen release from the NBAF, the impact assessment briefly mentions the possibility of introducing the agent into a natural reservoir that may sustain transmission. The committee finds this possibility was understated and is a concern regarding non-endemic agents that produce high mortality in animals and humans. The uSSRA discusses work that will be conducted at the NBAF to determine whether henipaviruses can infect North American bat species, and the committee concurs that such work is important. However, if henipaviruses affect native bat populations, this would affect the overall risk assessment and elevate the risk. There is also a potential for NiV to be introduced and transmitted in feral swine populations, which could be virtually impossible to control. Concerns about impact on native wildlife reservoirs should be part of a comprehensive risk assessment, but the uSSRA fails to fully address these risks to native wildlife reservoirs and their potential impact on animal and human health.

Human Illness

The committee finds that the uSSRA qualitatively understates aspects that deal with potential human illness. Particular concerns include (1) the ability and capacity of Mercy Regional Health Center to recognize and handle human illness associated with zoonotic pathogens held in the NBAF (such as NiV, HeV, and Rift Valley fever virus), and (2) the capabilities of the Kansas Department of Health and Environment (KDHE) and local health departments. It will be critical to quickly recognize and diagnose an infection caused by a BSL-4 agent, and the surveillance, diagnostic, and response capabilities of local and state partners may be insufficient for the NBAF in Manhattan, Kansas.

Similar to the previous committee, the present committee is concerned that the medical capabilities that are present at other locations with BSL-4 laboratories (e.g., Galveston and Atlanta) seem to be absent in Manhattan, Kansas. Although Mercy Regional Health Center has isolation rooms, the uSSRA states that there is only a single infectious disease physician and does not assess other medical capabilities in the area. Early recognition of a human zoonotic disease is crucial for proper treatment and could be the key in preventing a potential outbreak. For example, in 2000, a U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) scientist who was conducting research on *Burkholderia mallei*, the causative agent for glanders, was presented to a primary care physician with signs and symptoms consistent with glanders, but it took nearly two months for the proper diagnosis to be made (CDC, 2000). Similarly in 2009, it took at least two weeks for tularemia to be diagnosed in a USAMRIID researcher working with *Francisella tularensis* (Eckstein, 2009).

The ability of providers in the Manhattan area or other rural areas of Kansas to recognize the diseases caused by the suite of pathogens at the NBAF will need to be assessed and will likely need to be improved. The single infectious disease physician and the nursing staff and allied health professionals would be challenged to rapidly diagnose and provide the necessary care for patients with level 3 and 4 infections. HeV and NiV can have relatively long incubation periods, and NiV is known to be transmitted from person to person (Chadha et al., 2006; Gurley et al., 2007; Blum et al., 2009; Homaira et al., 2010). Although some BSL-4 agents are not stable in the environment and are difficult to transmit from person to person, the agent modeled in the uSSRA (NiV) has been transmitted through environmental exposures (from palm sap on trees) and has been transmitted from person to person in family and healthcare settings (Luby et al., 2009). Furthermore, humans are highly mobile (as noted in the FMDv portion of the uSSRA in which Biosecurity Research Institute personnel were questioned about mobility); therefore, patients could be present almost anywhere in Kansas or surrounding states. There may also be secondary cases that are not directly connected to the NBAF. For example, in 2006, a patient was presented to a major Washington, DC, hospital-affiliated primary care center with signs and symptoms of tularemia (a BSL-3 organism) but was not tested for the disease and was eventually discharged without further testing even though the patient informed the medical staff of the characteristic symptoms of tularemia infection (Dudley, 2010).

The uSSRA fails to fully consider the capabilities of KDHE and local health departments. Available information suggests that only emergency management officials in KDHE were contacted for the uSSRA. However, an unrecognized transference event involving human infection would require disease surveillance and diagnostic capacity that depend on KDHE epide-

miology and laboratory personnel more so than on emergency response personnel; this fact was overlooked in the uSSRA. Such capacities should have been assessed and modeled in the overall risk assessment.

Outbreaks involving either human or animal disease caused by a BSL-4 agent would almost certainly be a national problem rather than a regional one. Experience with other high-profile incidents—such as the incidents with anthrax in 2001 and severe acute respiratory syndrome (SARS) in 2003—demonstrates that although the overall number of domestic human cases was small, virtually all locations in the United States were required to investigate and test for potential illness once one case emerged (Perkins et al., 2002; CDC, 2003). If a domestically acquired case of HeV or NiV infection were recognized, there may be a nationwide investigation for disease prevalence in horses and pigs, respectively, but the qualitative portions of the uSSRA do not mention this. The uSSRA uses simple calculations to determine the cost of a human life or the cost of a pig or horse to estimate economic impact, but the costs associated with even a single case would be far greater than suggested due to the nature of the pathogen and the national attention that would ensue. The committee thus finds that the outbreak impact scoring (which is a relative weighting given the lack of a full quantitative analysis) provides false impressions of the impact of an accidental BSL-4 pathogen release from the NBAF.

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9

Overall Assessment, Findings, and Conclusions

The updated site-specific risk assessment (uSSRA) for the proposed National Bio- and Agro-Defense Facility (NBAF) released in 2012 is a substantial improvement over the original 2010 site-specific risk assessment (SSRA), and the Department of Homeland Security (DHS) and its contractors should be commended for this effort. Many of the shortcomings identified by the previous National Research Council committee (NRC, 2010) have been addressed in the uSSRA, and this has resulted in a more quantitative and transparent analysis. The uSSRA uses more conventional risk assessment methods and better complies with standard practice than did the 2010 SSRA. In general, the descriptions of the approaches are clear, and the uSSRA uses appropriate conceptual models and methods. However, the committee finds that some questionable and inappropriate assumptions were made to develop estimates of the probabilities, frequencies, and amounts of release of foot-and-mouth disease virus (FMDv) and other pathogens. In general, one needs to distinguish between the use of appropriate methods and use of appropriate assumptions to produce estimates. In the uSSRA, the former are generally acceptable, but the latter in some cases are not.

OVERALL ASSESSMENT

The quantitative conclusions of the uSSRA differ dramatically from those of the 2010 SSRA. Data and methods of the previous risk assessment led to a conclusion that for the two scenarios with the greatest risk of FMDv release (fomite and worker without respiratory protection), there

would be a 70% probability that FMDv release would cause an infection resulting in an outbreak during the 50-year life span of the NBAF in Manhattan, Kansas. In contrast, the uSSRA concludes that the cumulative probability for 142 risk events (including catastrophic events such as tornadoes and earthquakes) leading to an accidental release of FMDv over 50 years is about 0.11% (or 1 in 46,000 per year), which is orders of magnitude lower than the first estimate. Improvements in the 65% design phase documents for the facility compared with the earlier and less complete design documents on which the 2010 SSRA was based may explain some of the risk reduction. However, the committee believes that questionable and inappropriate assumptions were used in the uSSRA that led to artificially lower estimates of the probabilities and amounts of pathogen released.

In contrast with the 2010 SSRA, which cited fomites and lack of respiratory protection as the most likely pathways of accidental FMDv release, the uSSRA concludes that the most likely release mechanisms are those associated with natural hazards, specifically earthquakes and tornadoes. The uSSRA concludes that these are about 20 times more likely than operational pathways.

Despite improvements, the committee finds that the uSSRA underestimates the risks of pathogen release and infection and inadequately characterizes the uncertainties in those risks. The committee finds that the extremely low probabilities of release are based on overly optimistic and unsupported estimates of human error rates, underestimates of infectious material available for release, and inappropriate treatment of dependencies, uncertainties, and sensitivities in calculating release probabilities.

The committee is concerned that the vanishingly small estimates of risk found throughout the uSSRA are inconsistent with most modern, complex industrial systems. In many instances, the committee could not verify uSSRA results, because methods and data were unevenly or poorly presented. The uSSRA also contains inconsistent information, which made it difficult to interpret data or to reconstruct risk scenarios and thereby made it difficult to determine the degree to which risks were underestimated.

The committee recognizes that significant complexities accompany a risk assessment of this nature, yet the practice of risk analysis is sufficiently mature to be able to treat such complexities (Kumamoto and Henley, 1996; NASA, 2011) and therefore the committee's expectations for such a risk assessment are customary and attainable. The number of facilities comparable with the NBAF is small, so there is little empirical validation of the risk estimates. However, because a pathogen release from the NBAF could have devastating widespread agricultural, economic, and public health consequences, a risk assessment that reaches inappropriate conclusions could have substantial repercussions.

The committee has identified a number of deficiencies that lead to the conclusion that the uSSRA continues to be inadequate in characterizing the risks associated with operating the NBAF in Manhattan, Kansas.

FINDINGS

Congressional Mandate

Finding 1: The uSSRA addresses many, but not all, of the issues outlined in the congressional mandate. In 2010, a National Research Council committee found that the initial SSRA was not entirely adequate or valid, because of methodological limitations and assumptions that underestimated the risks and economic costs associated with an accidental FMDv release from the Manhattan, Kansas, site (NRC, 2010). The uSSRA attempts a quantitative risk assessment and attempts to model FMDv release and infection from the proposed NBAF in Manhattan, Kansas. However, it does not adequately include overall risks associated with the most dangerous pathogens in its biosafety level 4 (BSL-4) assessment.

65% Design Phase Plans for the National Bio- and Agro-Defense Facility

Finding 2: The 65% design phase plans for the facility appear to be sound. The NBAF design plans provided to the committee—which were at only 65% completion—appear to have been competently executed by architects and engineers experienced with modern biocontainment laboratories, and the designs appear to conform to international safety standards for similar facilities. Although DHS stated that those conducting the risk assessment consulted the building designs, the uSSRA does not seem to clearly reflect design changes or to incorporate such design provisions in the risk assessment (i.e., natural hazards assessments not reflecting 65% design plans that harden the structure against tornadoes). The committee recognizes that it is necessary and challenging to integrate design improvements to produce an informed risk assessment.

It is important to note that inadequacies in the uSSRA do not necessarily imply inadequacies in the design of the facility itself. Any conclusions about the adequacy and validity of the uSSRA should not be construed to imply similar conclusions with respect to the quality of the 65% design plans.

Use and Application of Risk Methods

Finding 3: The uSSRA misinterprets and misapplies some risk methods, which have implications for the entire risk assessment. The uSSRA adopts some risk assessment methods that are in line with current practice, including the application of event tree analysis and other methods of quantitative probabilistic risk assessment. The modeling framework used is a "scenario-based" approach that is a well-established approach to risk analysis of complex systems and processes. However, those risk assessment methods are inconsistently applied across the various sections of the report.

Lack of Independence Among Events and Parameter Values

Finding 4: The uSSRA ignores probabilistic dependencies in calculating risk scenarios, and this results in potentially serious underestimations of total risk and incorrect ranking of risk contributors. Use of questionable or erroneous methods and assumptions about probabilistic dependencies in portions of the uSSRA most likely results in an underestimation of the probability of accidental FMDv release.

In probabilistic modeling, it is fundamentally important to correctly characterize probabilistic dependencies among events and model parameters, and to account for dependencies in calculating probabilities of the joint occurrence of those events and parameters. The uSSRA assumes that all events are probabilistically independent of each other whereas in reality they can be dependent. Failure to consider the possibility that many event sequences could contribute to loss of containment and subsequent infections is an important deficiency and could lead to a serious underestimation of risk.

Uncertainty and Sensitivity Analysis

Finding 5: The characterization and assessment of uncertainties are incomplete and inconsistent, and this leads to a false sense of precision. Sensitivity analyses and a quantitative assessment of the uncertainties in key model assumptions, model parameters, and risk results are required for the uSSRA to be viewed as adequate. A thorough view of uncertainties is necessary for sound decision making. Except for the epidemic modeling section, the uSSRA does not consider that there are large differences in the quality and quantity of data and information used to support the analysis or how those differences could affect the reliability of subsequent risk estimates. The only measure of "uncertainty" identified in the uSSRA (Section 8) is "stochastic variability." There appears

to be no comprehensive consideration of epistemic uncertainty related to lack of data or knowledge, and the cumulative effects of uncertainty on the overall assessment are not adequately discussed.

Sensitivity analyses, which would be a way to examine the effects of model assumptions and variations in parameter values, are not comprehensive and in most cases do not adequately test the effects of the range of variability of the model parameters. The lack of full assessment of uncertainties is a serious deficiency in the uSSRA and limits its utility for decision making.

Treatment of Human Reliability and Human Error

Finding 6: The uSSRA applies very low human error rates and uses methods that omit important error pathways, which likely resulted in low estimated probabilities of release. Probabilities of human error used in the uSSRA appear not to be based on published literature or empirical experience. The 2010 SSRA concluded that human error would be the most likely cause of release, and the previous committee agreed with that conclusion (Finding 9 of NRC, 2010). Little justification is provided for the uSSRA's optimistic assumption that, in at least one pathway, the rate of human error for NBAF workers will be several times less than that of similarly skilled workers in similar facilities. Furthermore, not all pathways by which human error can be a significant factor in failure modes have been satisfactorily considered.

Human error is an important contributor to risk in facilities similar to the NBAF. The uSSRA should have explored possible sources of data and operating experience for human error in analogous research laboratory settings as the basis of reference error probabilities.

Modeling Parameters and Assumptions

Finding 7: The uSSRA appears overly optimistic in its assignment of parameter values to models, yet describes the values as conservative. Underestimates of parameter values by one or two orders of magnitude—when taken together in multiplicative estimation—can lead to extremely low compound estimates of risk. This is significant because while a bias of one order of magnitude in central tendency appears minor, the presence of several such biases in sequence will shift the final results by many orders of magnitude. While this problem is not apparent throughout the report, the lack of an adequate sensitivity analysis makes it difficult to ascertain the effects on estimated risks of the alternative assumptions used.

Finding 8: The uSSRA does not describe the approaches used to ensure thoroughness in the review of parametric inputs. Therefore, it is impossible to determine whether the scientific literature and other information used to support risk assessment assumptions have been thoroughly reviewed and evaluated. Many parameter estimates depend on outdated references or on only a single reference. In many places, the uSSRA appears to use unrealistic assumptions to determine model parameters, and the parameter values that were adopted appear to be inconsistent among sections and even within sections of the report. Within sections of the report, parameter values given in the text and in tables are in apparent conflict. At times, the uSSRA selects the lowest resulting risk input factors despite the availability of other data yielding a higher risk.

Finding 9: The uSSRA has improved its epidemic modeling to address previous criticisms; however, there continue to be significant limitations in model capabilities and available data, leaving large uncertainties in the numbers provided. Particular assumptions likely led to an underestimation of the magnitude of spread and the duration of an FMD outbreak that would result from an FMDv release from the NBAF in Manhattan, Kansas. The uSSRA did not consider the possibility that an FMD outbreak could quickly spread out of control in the United States and result in FMD becoming an endemic disease that requires a very long-term eradication program.

Finding 10: Although the methods used for the economic analysis are appropriate, the uSSRA does not provide sufficient information to replicate the results or to assess whether the analysis was properly executed. Underestimates of the magnitude, spread, and duration of an FMD outbreak were carried over into the economic model and led to a likely underestimate of the economic consequence of an FMDv escape from the NBAF.

Treatment of Natural Hazards

Finding 11: The committee questions the conclusion that catastrophic natural hazards pose the greatest risk for accidental release of FMDv and finds that the uSSRA overestimates their probabilities. Despite eastern Kansas being a region of relatively low seismicity, the uSSRA designates earthquakes as the hazard most likely to lead to an FMDv release from the Manhattan, Kansas, facility. Tornadoes are a more significant natural hazard, given the proposed location of the NBAF in an area with a disproportionately high frequency of tornadoes known as "Tornado Alley."

One reason for DHS's conclusion is that the uSSRA uses an annual exceedance probability of a 1-second ground shaking as the defining hazard, whereas a low-rise structure like the NBAF is mostly susceptible to a shorter period event. This results in an exceedance probability that is higher by perhaps a factor of 20 than what should have been used and inflates the earthquake hazard risk estimates. Furthermore, the uSSRA does not account for the low structural fragility (strong resistance) of the proposed design, so the probability of a release is overestimated by perhaps several orders of magnitude.

For tornado loading, the hazard is estimated (e.g., probability of exceedance of tornado winds above certain speeds), but again the facility's low structural fragility to those winds is not considered. That leads to overestimation of the risk of releases due to tornadoes by implicitly assuming that any wind above a particular speed leads to a release of 100% of the material available for release. Thus, the committee considers the estimates of the probability of releases due to both natural hazards to be too high.

Surveillance, Response, and Mitigation Plans

Finding 12: The uSSRA is based on assumptions about surveillance, detection, response, and mitigation strategies that were not adequately comprehensive or science-based. Also it appears they were developed with insufficient input from stakeholders and federal, state, and local governments. Assumptions used to model mitigation, response, and detection were based in large part on DHS and USDA expectations for significantly improved plans, programs, and strategies that would be implemented by the time the NBAF opens in 2020. Surveillance, detection, and emergency response capabilities (such as vaccine availability) are critical for mitigating an outbreak, yet those tools and capabilities are currently limited or not in place. There was no indication from DHS or USDA that the necessary science-based capabilities noted by the previous committee (Finding 7 in NRC, 2010) would be implemented for FMD surveillance and response.

DHS and USDA still have significant gaps for providing these critical capabilities and for realistically carrying out plans that identify and incorporate agricultural, animal health, and public health sectors and major issues related to a potential pathogen release. DHS and USDA have experience operating similar facilities such as the National Biodefense Analysis and Countermeasures Center (NBACC) and Plum Island Animal Disease Center (PIADC), which could have helped to supplement the uSSRA in providing robust plans for the development of emergency response capabilities. Similarly, local and state emergency

response, healthcare, and related organizations have significant gaps that the uSSRA assumes will be filled by the time the facility opens, but for which a comprehensive timeline has not been provided. Therefore, it is difficult to know whether the calculations and conclusions in the uSSRA regarding spread and impact are adequate and valid. If these assumed plans, programs, and strategies are not fully developed, validated, and implemented by the time the NBAF opens in 2020, the risks and consequent impacts will likely be substantially greater than estimated in the uSSRA.

Personnel Preparedness and Training

Finding 13: The uSSRA does not adequately address plans for personnel preparedness and training at the NBAF. Although the training and preparedness requirements of the Federal Select Agent Program established under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 are well documented, the uSSRA fails to include the DHS plans for personnel training in security, laboratory procedures, and emergency response as required by P.L. 112-10. Those plans are critical for ensuring safe operations at the NBAF and for mitigating an accidental FMDv release from the laboratory. As previously mentioned, DHS and its contractors could have drawn from experiences of operating similar facilities like NBACC and PIADC to inform plans for NBAF personnel training and standard operating procedures. Exclusion of such information from the uSSRA leads the committee to believe that preparations for the requirement have not been fully addressed by DHS.

BSL-4 Assessment

Finding 14: In the BSL-4 assessment, the uSSRA does not consider overall risk and presents a limited qualitative assessment of impact. Such an evaluation likely underestimates the overall risk related to the BSL-4 suite, and the potential impact of a release cannot be evaluated. The committee recognizes the inherent limitations in the available information regarding the henipaviruses that form the basis of the BSL-4 review and other agents that may be studied in the BSL-4 suite. However, the risk assessment focuses only on the *unique* risks of release from the BSL-4 suite associated with the use of large animals.

The uSSRA does not adequately consider the totality of risks in its BSL-4 assessment. An overall risk assessment of the NBAF BSL-4 would need to include an evaluation of the *additive* risks associated with the entire array of BSL-4 work. That includes the risk of a release

from the BSL-4 associated with use of large animals in the BSL-4 suite, the risk of a release associated with non-animal-related activities in the BSL-4 suite, and the risk of a release from the BSL-4 suite associated with natural disasters. The epidemiological and economic impacts of such a release would then be evaluated as part of the risk assessment.

The uSSRA includes a semi-quantitative risk assessment of the two exclusively BSL-4 agents on the priority list for work at the NBAF: Hendra virus and Nipah virus. The uSSRA states that the primary objective of the BSL-4 risk assessment is "to identify and characterize the unique risks associated with working with large animals in BSL-4 conditions". As a result, the analysis focuses exclusively on risks associated with handling of infected large animals in BSL-4 containment. That suggests that all other activities in the BSL-4 suite are risk-free, which is not the case. As a result, the approach used for the BSL-4 evaluation understates the range of potential risks in the BSL-4 environment.

LIMITED APPLICABILITY OF THE UPDATED SITE-SPECIFIC RISK ASSESSMENT

For any risk assessment, results apply only when the assumptions upon which they are based are consistent with practice. The uSSRA makes key assumptions about the physical design of the facility, maintenance and operation, and implementation of mitigation strategies. Any significant deviation from the assumed characteristics will modify risk factors and reduce the validity of the risk assessment.

It is critical to recognize that a sufficient level of funding for the NBAF and for risk mitigation activities is required to carry out the planned assumptions noted in the uSSRA. Operating BSL-3 and especially BSL-4 facilities is expensive because of equipment, personnel, operating costs, and maintenance and because of the need for systems for detection and active surveillance. Shortcomings in any of those areas will impact the risk profile of the facility. Without a long-term funding commitment that is sufficient to maintain the level and quality of NBAF operations and that can sustain planned mitigation strategies, the findings presented in the uSSRA are not assured.

Not all deviations from the planning assumptions would significantly alter risk. If the uSSRA had included a careful sensitivity analysis based on alternative assumptions and if the deviations had been captured in such a sensitivity analysis, the uSSRA might still be applicable. The uSSRA provided to the committee contains no such sensitivity analysis. The uSSRA has limitations in its applicability, and these limitations are not clearly stated in the uSSRA. Absent a thorough sensitivity analysis, the applicability of the uSSRA under alternative operational conditions cannot be ascertained.

CONCLUSIONS

It is important to note that research, diagnostic, and mitigation capabilities envisioned for the NBAF are critical for protecting the nation against known threat agents along with emerging and unknown disease threats. The present committee echoes the conclusions of previous NRC committees that the United States needs the capacity to support critical research and diagnostic programs for the study of foreign animal diseases and zoonotic diseases that are directly linked to securing the health and wealth of the nation (NRC, 2005a,b, 2010; IOM and NRC, 2009).

As required by P.L. 112-10, the committee was instructed to judge the adequacy and validity of the uSSRA. The committee has identified serious concerns about (1) the misapplication of methods used to assess risk, (2) the failure to make clear whether and how the evidence used to support risk assessment assumptions had been thoroughly reviewed and adequately evaluated, (3) the limited breadth of literature cited and the misinterpretation of some of the significant supporting literature, (4) the failure to explain the criteria used to select assumptions when supporting literature is conflicting, (5) the failure to consider important risk pathways, and (6) the inadequate treatment of uncertainty. Those deficiencies are not equally problematic, but they occur with sufficient frequency to raise doubts about the adequacy and validity of the risk results presented. In most instances (e.g., operational activities at the NBAF), the identified problems lead to an underestimation of risk; in other instances (e.g., catastrophic natural hazards), the risks may be overestimated. As a result, the committee concludes that the uSSRA is technically inadequate in critical respects and is an insufficient basis on which to judge the risks associated with the proposed NBAF in Manhattan, Kansas.

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Appendixes

Appendix A

Committee Biosketches

Gregory B. Baecher (Chair) is the Glenn L. Martin Institute Professor of Engineering at the University of Maryland. His research focuses on the reliability of civil infrastructure and risks posed by natural hazards and the response of infrastructure to those hazards. In recent years, his research has dealt with dam safety and with the response of levee systems to flooding, including actuarial issues related to flood and other natural hazard insurance. He has also worked on quantitative methods in facilities management, especially federally owned facilities, and on information technology applications to facilities management. Dr. Baecher was elected to the National Academy of Engineering in 2006 for his work in the development, explication, and implementation of probabilistic- and reliability-based approaches to geotechnical and water-resources engineering. He is a recipient of the Commander's Award for Public Service from the U.S. Army Corps of Engineers and a recipient of the Thomas A. Middlebrooks Award and State-of-the-Art Award from the American Society of Civil Engineers. He is co-author of *Reliability and Statistics in Geotechnical Engineering* (2003), *Risk and Uncertainty in Dam Safety* (2004), and *Protection of Civil Infrastructure from Acts of Terrorism* (2006). Dr. Baecher received his Ph.D. and M.Sc. degrees from the Massachusetts Institute of Technology and his B.S.C.E. from the University of California at Berkeley.

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 investi-

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gator 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 on 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 received his Ph.D. in environmental engineering and M.S. in environmental health from Drexel University.

Richard E. Breitmeyer was appointed director of the California Animal Health and Food Safety Laboratory System in November 2010. Operating under the administration of the University of California at Davis (UC Davis) School of Veterinary Medicine, the laboratory system is the backbone of California's animal disease surveillance and detection system and is used to safeguard human and animal health from naturally occurring or intentionally introduced animal diseases by rapidly and reliably diagnosing diseases found in animals. Before joining UC Davis, Dr. Breitmeyer had a 26-year career with the California Department of Food and Agriculture (CDFA), serving as California's state veterinarian from 1993 to 2010. As state veterinarian, he had the statutory authority to quarantine domestic animals or food to protect the health and safety of animals and the public. From 1993 to 2004, Dr. Breitmeyer also served as the director of Animal Health and Food Safety Services and oversaw an annual budget of $30 million and 250 employees engaged in programs for animal health, milk and dairy foods control, meat and poultry inspection, and livestock identification. Before joining CDFA, he was a private practitioner in Humboldt and San Luis Obispo counties. Dr. Breitmeyer is an active member of many state and national organizations and is the immediate past president of the United States Animal Health Association. He also served for 10 years on the Secretary of Agriculture's Advisory Committee for Foreign Animal and Poultry Diseases. Dr. Breitmeyer received his D.V.M. and M.P.V.M. degrees from UC Davis, and he conducted his undergraduate studies at California Polytechnic State University, San Luis Obispo.

Corrie C. Brown is the Josiah Meigs Distinguished Teaching Professor in the College of Veterinary Medicine at the University of Georgia. Her research includes the study of pathogenesis of infectious disease in food-

producing animals through the use of immunohistochemistry and in situ hybridization. She is active in the fields of emerging diseases and international veterinary medicine and serves as coordinator of international activities for the College of Veterinary Medicine. Before joining the University of Georgia in 1996, she worked at the U.S. Department of Agriculture (USDA) Plum Island Foreign Animal Disease Center for 10 years, conducting pathogenesis studies on many foreign animal diseases. Her bench research at the University of Georgia has focused on poultry diseases, and she works closely with the USDA facility in Athens that is dedicated to foreign diseases of poultry. In educational research, she has several grants to promote national animal health infrastructure in developing nations. Dr. Brown is a Diplomate of the American College of Veterinary Pathologists. She has published or presented more than 250 scientific papers and has testified before Congress on issues involving agroterrorism. Dr. Brown has served on many industrial and federal panels and has been a technical consultant to numerous foreign governments on issues involving infectious diseases and animal health infrastructure. She received her Ph.D. in veterinary pathology with a specialization in infectious diseases from the University of California at Davis and her D.V.M. from the University of Guelph.

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. His 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. He received his Ph.D. and M.S. in environmental engineering and his B.S. in civil engineering from the University of California at Berkeley.

Ahsan Kareem is the Robert M. Moran Professor of Engineering and the director of the NatHaz Modeling Laboratory at the University of Notre Dame. His research uses computer models and laboratory and full-scale experiments to study the dynamic effects of environmental loads under winds, waves, and earthquakes to understand and predict the impact of natural hazards on the constructed environment, and to develop mitigation strategies that enhance the performance and safety of structures. He is a former president of the American Association for Wind Engineering and past editor-in-chief of the international journal *Wind and Structures*.

Dr. Kareem is the recipient of the Alan G. Davenport Medal presented by the International Association for Wind Engineering in recognition of his distinguished achievement in dynamic wind effects on structures and of the Robert H. Scanlan Medal for outstanding contributions to the study of aeroelasticity/aerodynamics and wind-load effects on structural design and the Jack E. Cermak Medal in recognition of his contributions to the understanding of wind effects on structures from the American Society of Civil Engineers (ASCE). Dr. Kareem was elected to the National Academy of Engineering in 2009 for his contributions to analyses and designs to account for wind effects on tall buildings, long-span bridges, and other structures. In 2010, he was elected a foreign fellow of the Indian National Academy of Engineering and elected a distinguished member of ASCE for his knowledge and eminence in the field of wind engineering, structural engineering, and engineering mechanics; for his contributions to the ASCE Wind Loads Standards; and for his development of Web-based technologies and design tools for practice. Dr. Kareem received his Ph.D. in civil engineering from Colorado State University, M.Sc. in civil engineering from the University of Hawaii, and B.Sc. in civil engineering from West Pakistan University of Engineering and Technology.

Brendan McCluskey was appointed 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 biosafety level 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 New Jersey Governor's Task Force on Campus Safety 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 on 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. He received his J.D. from Rutgers University School of Law and his B.A. and M.P.A. from Kean University.

Ali Mosleh holds the Nicole J. Kim Eminent Professor of Engineering Chair and is the director of the Center for Risk and Reliability at the University of Maryland. He conducts research on methods for probabilistic risk analysis (PRA) and reliability of complex systems. He has made many contributions

in diverse fields of theory and application, including Bayesian methods of inference with uncertain evidence; analysis of data and expert judgment; treatment of model uncertainty; risk and reliability of hybrid systems of hardware, human, and software; methods and tools for dynamic PRA; cognitive models for human reliability analysis; and models of the influence of organizational factors on system reliability and safety. Dr. Mosleh has led numerous projects on reliability, risk, safety, and security assessments for the aerospace, nuclear, chemical, and information systems industries. In 2004, Dr. Mosleh was appointed by President George W. Bush to the U.S. Nuclear Waste Technical Review Board, a position in which he continues to serve in the administration of President Barack Obama. He is an elected member of the National Academy of Engineering, a fellow of the Society for Risk Analysis, recipient of several scientific achievement awards, and a consultant and technical adviser to national and international organizations. Dr. Mosleh received his Ph.D. in nuclear science and engineering from the University of California at Los Angeles.

Stephen M. Ostroff is the acting physician general for the Pennsylvania Department of Health. In this role, he partners with public health professionals on matters related to department programs and executive branch agencies and reviews standards and practices of medicine in the jurisdiction of the department. Dr. Ostroff acts as the primary adviser on medical issues to both the secretary of health and the governor and represents the department before the General Assembly, the press, medical professionals, and community and citizens groups. In addition to functioning as the acting physician general, he has been the director of the Bureau of Epidemiology since 2007. Before his retirement from the Centers for Disease Control and Prevention (CDC), Dr. Ostroff was the assistant surgeon general and deputy director of the National Center for Infectious Diseases from 2002 to 2005, where he coordinated activities related to outbreak investigations, antimicrobial resistance, and bioterrorism. From 2001 to 2003, he served as acting director of CDC's Select Agents program, and from 2001 to 2005, he served as president of the Department of Defense Armed Forces Epidemiology Board. Dr. Ostroff is also the immediate past president of the Council of State and Territorial Epidemiologists and serves on CDC's Healthcare Infection Control Practices Advisory Committee. During his career, he has authored over 80 peer-reviewed articles and book chapters on emerging infectious diseases and has testified before Congress on a number of occasions. Dr. Ostroff received his M.D. from the University of Pennsylvania School of Medicine and completed residencies in internal medicine at the University of Colorado Health Sciences Center and in preventive medicine at CDC.

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 in the U.S. Department of Agriculture (USDA) Economic Research Service (ERS) from 1977 to 1985, 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 Ph.D. thesis, and an award for outstanding journal article for 2003 from the Southern Agricultural Economics Association. Dr. Paarlberg received his Ph.D. and M.S. degrees in agricultural economics and B.A. 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. in applied mathematics from the University of Washington and his B.S. in biology and mathematics from Tufts University.

Joseph V. Rodricks is a founding principal of ENVIRON and a visiting professor at the Johns Hopkins Bloomberg School of Public Health. He is an internationally recognized expert in the field of toxicology and risk analysis. Since 1980, Dr. Rodricks has consulted for hundreds of manufacturers, government agencies, and the World Health Organization in the evaluation of health risks associated with human exposure to chemical substances. His experience includes chemical products and contaminants in foods, food ingredients, air, water, hazardous wastes, the workplace, consumer products, medical devices, and pharmaceutical products. Dr. Rodricks was formerly deputy associate commissioner for health affairs and a toxicologist at the U.S. Food and Drug Administration (1965–1980). He has served on 25 boards and committees of the National Research Council and the Institute of Medicine, including the committees that produced the

seminal works *Risk Assessment in the Federal Government: Managing the Process* (1983) and *Science and Decisions: Advancing Risk Assessment* (2009). He has more than 200 publications on toxicology and risk analysis and is the author of *Calculated Risks* (Cambridge University Press), a non-technical introduction to toxicology and risk analysis that is now available in a fully revised and updated second edition, for which he won an award from the American Medical Writers Association. Dr. Rodricks received his Ph.D. in biochemistry and M.S. in organic chemistry from the University of Maryland and his B.S. in chemistry from the Massachusetts Institute of Technology.

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 of Iowa State University and 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 has served on the Interagency Weapons of Mass Destruction Counter Measures Working Group Animal Pathogen Research and Development Subgroup, and the White House Office of Science and Technology Policy Blue Ribbon Panel on the Threat of Biological Terrorism Directed Against Livestock. He is a Diplomate of the American College of Veterinary Microbiologists. Dr. Roth received his Ph.D. and M.S. in veterinary microbiology, and his D.V.M. from Iowa State University.

Lee H. Thompson is the director of institutional biocontainment resources and an assistant professor of pathology at the University of Texas Medical Branch at Galveston (UTMB). As the director of institutional biocontainment at UTMB, he oversees the physical operations of the biosafety level 3 and 4 (BSL-3 and BSL-4) facilities, develops policies and procedures relevant to safety for the facilities, and provides guidance on facility construction and renovation projects. He has also monitored the construction and commissioning activities for the BSL-4 facility at UTMB. Before his appointment at UTMB, he was invited by the Canadian minister of health to serve as the chief of safety and environmental services for the Canadian Science Centre for Human and Animal Health in Winnipeg. In that role, he provided advice on construction and commissioning of the BSL-3, BSL-3Ag, and BSL-4 facilities and developed the standard operating procedures for activation, operation and maintenance, safety, and training. Mr. Thompson

has also served as an invited design and biosafety consultant for a number of BSL-4 laboratories, including those at the National Institute of Allergy and Infectious Diseases in Ft. Detrick, Maryland, and at the Rocky Mountain Laboratories in Hamilton, Montana. Before retiring from the U.S. Department of Agriculture, he was microbiologist and safety director in the arthropod-borne animal disease research laboratory with the Agricultural Research Service, where he conducted research on insect-transmitted viral diseases of ruminants and was responsible for biological safety, facility design, operation, and security in containment. Mr. Thompson received his B.S. in microbiology from Metropolitan State College in Denver, Colorado.

Mark C. Thurmond is professor emeritus of veterinary epidemiology in the Department of Medicine and Epidemiology in the School of Veterinary Medicine at the University of California at Davis (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 Foot-and-Mouth Disease Surveillance and Modeling Laboratory, where he continues to pursue his research interests in infectious disease epidemiology and surveillance, particularly as related to foot-and-mouth disease. His interests during the last 40 years of professional teaching, research, and service have included clinical medicine and clinical epidemiology, primarily related to infectious diseases of livestock, new methods for diagnostic epidemiology, and modeling and developing disease control and surveillance systems. His clinical practice focused mainly on provision of herd health programs and service to the dairy industry. Dr. Thurmond received his Ph.D. in dairy science and epidemiology from the University of Florida and his D.V.M. and M.P.V.M. 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 Modeling System (SOMS). He was a member of the committee that developed the American Meteorological Society–Environmental Protection Agency (AMS/EPA) Regulatory Model (AERMOD), which has replaced ISC as EPA's regulatory model. He now serves on an EPA committee that is charged with overseeing the improve-

ment of AERMOD. 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 currently 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 in the Atmospheric Environment Service, Canada, for a year before joining the Ontario Ministry of the Environment, Toronto. Dr. Venkatram received his Ph.D. in mechanical engineering from Purdue University and his B.S. in mechanical engineering from the Indian Institute of Technology in Madras, India.

Patrick M. Webb is the director of swine health programs at the National Pork Board, which he joined in 2005. He is responsible for the Pork Check-off's efforts in animal identification, pre-harvest traceability, and foreign animal disease planning, preparedness, and response. Earlier, Dr. Webb worked as a private veterinary practitioner in a food animal practice in rural Iowa. He has also worked for Iowa's Department of Agriculture and Land Stewardship as a foreign animal disease program coordinator, where he developed the department's emergency preparedness plan for animal disease disasters. Throughout his career, Dr. Webb has worked extensively on emergency preparedness and planning at the local, state, and federal levels. He has developed and delivered numerous educational programs directed at training producers, veterinarians, county emergency managers, and first responders in how to react to foreign animal disease disasters. He completed his training at the Foreign Animal Disease Diagnostic Laboratory at Plum Island. Dr. Webb is a member of the American Association of Swine Veterinarians, the Iowa Veterinary Medical Association, and the American Veterinary Medical Association. He received his D.V.M. and B.S. in animal science from Iowa State University.

Appendix B

Meeting Agendas and Lists
of Public Participants

MEETING 1
AGENDA

September 6-7, 2011
Keck Center of the National Academies
Washington, DC

Tuesday, September 6

12:30 – 12:45 p.m.	Welcome and Introductions *Greg Baecher (Chair)*
12:45 – 1:10 p.m.	Remarks about the NBAF *Cathie Woteki (Undersecretary for Research, Education, and Economics, U.S. Department of Agriculture)*
1:10 – 2:00 p.m.	Overview of the NBAF and Proposed Updates for the SSRA *Jamie Johnson (Director, Office of National Laboratories (ONL), U.S. Department of Homeland Security (DHS))* *Julie Brewer (NBAF Project Manager, ONL, DHS)*
2:00 – 2:20 p.m.	Q&A *Moderator: Greg Baecher (Chair)*
2:20 – 2:50 p.m.	Overview of NBAF Design Updates *Eugene Cole (NBAF Technical Design Lead)*

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2:50 – 3:00 p.m.   Q&A
                          Moderator: Greg Baecher (Chair)

3:00 – 3:15 p.m.   Break

3:15 – 5:15 p.m.   Session 1: Risk Scenarios
                          Lead Presenter: Adam Hamilton (Signature Science)
                          Moderator: Greg Baecher (Chair)

5:15 – 5:45 p.m.   Public Comments
                          Please register ahead of time

5:45 p.m.   Adjourn Open Session

Wednesday, September 7

8:30 – 8:40 a.m.   Welcome and Recap of Day 1
                          Greg Baecher (Chair)

8:40 – 10:30 a.m.   Session 2: Epidemiological Modeling &
                          Emergency Response Planning
                          *Lead Presenter: Rocco Casagrande (Gryphon
                          Scientific)*
                          Moderator: Greg Baecher (Chair)

10:30 – 10:45 a.m.   Break

10:45 a.m. – 12:15 p.m.   Session 2: Epidemiological Modeling &
                          Emergency Response Planning (cont'd)
                          *Lead Presenter: Rocco Casagrande (Gryphon
                          Scientific)*
                          Moderator: Greg Baecher (Chair)

12:15 – 1:00 p.m.   Lunch
                          (Working lunch for committee members and
                          committee's invited guests;
                          Others will have lunch on their own)

1:00 – 2:30 p.m.   Session 3: Risk Calculations
                          Lead Presenter: Molly Isbell (Signature Science)
                          Moderator: Greg Baecher (Chair)

2:30 – 2:50 p.m.	Break & Relocate to Room 110
	Live videocast in overflow room, Room 105
2:50 – 4:20 p.m.	Session 4: Semi-Quantitative Risk Assessment
	Lead Presenter: Dana Kadavy (Signature Science)
	Moderator: Greg Baecher (Chair)
4:20 – 4:30 p.m.	Public Comments & Closing Remarks
	Please register ahead of time
	Greg Baecher (Chair)
4:30 p.m.	Adjourn Open Session

MEETING 1
LIST OF PUBLIC PARTICIPANTS

Tammy Beckham, Texas Veterinary Medical Diagnostic Laboratory
Steve Bennett, U.S. Department of Homeland Security
Paul E. Bieringer, STAR, LLC
Julie S. Brewer, U.S. Department of Homeland Security
Naeem N. Brewington, U.S. Department of Homeland Security
Frank Bryant, SES, Inc.
Rocco Casagrande, Gryphon Scientific
L. Eugene Cole II, U.S. Department of Homeland Security
Kimberly Forde-Folle, U.S. Department of Agriculture
Landon Fulmer, National Bio- and Agro-Defense Facility Kansas Steering
     Committee
Cyril G. Gay, U.S. Department of Agriculture
Charles Haas, Drexel University
Adam L. Hamilton, Signature Science, LLC
Molly Isbell, Signature Science, LLC
Michael A. Johnson, Institute for Animal Health
James Johnson, U.S. Department of Homeland Security
Joanne Jones-Meehan, U.S. Department of Homeland Security
Dana R. Kadavy, Signature Science, LLC
Mark Kazmierczak, Gryphon Scientific
Joe Kozlovak, U.S. Department of Agriculture
Christopher F. Kronser, FLAD Architects
Thomas G. Ksiazek, Galveston National Laboratory
Paul Langevin, Merrick and Company
Elizabeth Lautner, U.S. Department of Agriculture
Justin Lyon, Natural Systems International
Thomas L. Marsh, Washington State University

Thomas Mettenleiter, Friedrich-Loeffler-Institut
Gay Miller, University of Illinois, Urbana
Michael Moreland, Perkins & Will
Mark Mussante, Citizen
Theda Owens, Office of Senator Pat Roberts (R-KS)
Gregory Paoli, Risk Sciences International
Dustin Pendell, Colorado State University
Jon Peterka, CPP, Inc.
Sue Peterson, Kansas State University
Greg Pompelli, U.S. Department of Agriculture
Sharla Rausch, U.S. Department of Homeland Security
Margaret Rush, Gryphon Scientific
Michael W. Sanderson, Kansas State University
Barrett Slenning, North Carolina State University
Greg Smith, Australian Animal Health Laboratory
Patrick Splichal, SES, Inc.
Wayne Stoskopf, Office of Congresswoman Lynn Jenkins (R-KS)
Sara Szmania, Signature Science, LLC
Alfonso Torres, Cornell University
Ron Trewyn, Kansas State University
Neal Woollen, United States Army
Catherine E. Woteki, U.S. Department of Agriculture
Anne Marie Zaudtke, U.S. Department of Homeland Security

MEETING 2
AGENDA

November 8-9, 2011
Keck Center of the National Academies
Washington, D.C.

Tuesday, November 8

9:00 a.m.   Welcome

9:15 a.m.   Design Document Briefing from DHS via
                       teleconference

9:45 a.m. – 7:30 p.m. Closed session (committee and staff only)

Wednesday, November 9

9:00 a.m. – 5:00 p.m. Closed session (committee and staff only)

MEETING 3
AGENDA

January 27, 2012
Kansas State University
Manhattan, Kansas

8:00 a.m.	Welcome, Introductions, and Purpose of the Meeting *Gregory Baecher (chair)*
8:07 a.m.	Opening Remarks *Ron Trewyn (Vice President of Research, Kansas State University)*
8:10 a.m.	Q&A Discussion with K-State faculty and researchers about NBAF *Committee* *Moderator: Gregory Baecher (chair)*
9:05 a.m.	Public Comments Please sign-up in advance *Moderator: Gregory Baecher (chair)*
9:55 a.m.	Concluding Remarks *Gregory Baecher (chair)*
10:00 a.m.	Adjourn public meeting

MEETING 3
LIST OF PUBLIC PARTICIPANTS

Gary Anderson, Kansas State University
Stephen Anderson, Citizen
Ty Arneson, Junction City Area Chamber of Commerce
Timothy Barr, U.S. Department of Homeland Security
Richard Beeman, U.S. Department of Agriculture
Sylvia Beeman, Citizen
Joe Blackford, MRIGlobal
Susan Blackford, Citizen
Frank Blecha, Kansas State University
Beth Bohn, Kansas State University

Brandon Bohning, Congressional Aide
Shirley Boweb, Wabaunsee County Land Owner
Julie S. Brewer, U.S. Department of Homeland Security
John Broberg, Mercy Regional Health Center
Jessica Brooks, Kansas State University
William Brown, Kansas Department of Agriculture
Myron Calhoun, Riley County
Leslie Campbell, Kansas State University Student
James Carpenter, Kansas State University
M.M. Chengappa, Kansas State University
Peter Cohen, Wabaunsee County Planning Commission
Suzanne Cohen, Citzen
Pat Collins, Riley County
Anne Cowan, Manhattan Alliance for Peace and Justice
Sandy Cravens, Citizen
Trevor Davis, Kansas State University
Alejandra Desormack, Citizen
Torry Dickinson, Kansas State University
William Dorsett, Citizen
Janell Dowling, Citizen
Barbara Drolet, U.S. Department of Agriculture
Ronnie Elmore, Kansas State University
Ron Fehr, Manhattan City Manager
Roger Fingland, Kansas State University
Daniel Fredhorn, Citizen
Landon Fulmer, National Bio- and- Agro-Defense Facility Kansas Steering
    Committee
Patrick Gormley, Kansas State University
Ronnie Grice, Kansas State University
James Guikema, Kansas State University
Kasandra Gurther, Citizen
Dave Guthals, Riley County
Kenneth Harkin, Kansas State University
Brad Hartenstein, RSC Equipment Rental
Dick Hesse, Kansas State University
Stephen Higgs, Biosecurity Research Institute
Marvin Hitschmann, Citizen
Stan Hoerman, Citizen
Clancy Holeman, Riley County Counselor
Jerry Jaax, Kansas State University
Susan Jagerson, Junction City Area Chamber of Commerce
Alvan Johnson, Riley County Clerk's Office
Seth Kelso, McCarthy Building Companies

George Kennedy, Kansas State University
Mike Kenney, Kansas State University
Susanne Kufahl, Riley County Health Department
Tom Leopold, Citizen
Lance Luftman, Biosecurity Research Institute
Wenjun Ma, Kansas State University
David MacFarland, Retired - Kansas State University
Monta Manney, Kansas State University
Thomas Manney, Kansas State University
Cheryl May, Kansas State University
Michael McNulty, Kansas Department of Health and Environment
Sara McReynolds, Kansas State University Student
Scott McVey, U.S. Department of Agriculture
Jeff Morris, Kansas State University
Rebecca Mosier, Citizen
Nancy Muturi, Kansas State University
Debbie Nuss, Citizen
Charles Oviatt, Citizen
Susan Oviatt, SBC Global
Loren Pepperd, Commissioner of Manhattan, Kansas
Sue Peterson, Kansas State University
Marjorie Pfister, Citizen
Stephen Pfister, Citizen
Karen Rappoport, Citizen
Ralph Richardson, Kansas State University
Juergen Richt, Kansas State University
William Richter, Kansas State University
Bob Rowland, Kansas State University
Bonnie Rush, Kansas State University
Scott Rusk, Biosecurity Research Institute
Mike Sanderson, Kansas State University
Robert Schaeffer, Kansas State University
Debra Schaub, Kansas State Department of Commerce
Mark Scott, Loundon County Federal Bureau
Scott Shoemaker, Sunset Zoo
Donna Smith, Citizen
Jennifer Tidball, Kansas State University
R.W. Trewyn, Kansas State University
Chris Trudo, Pottawatomie County Emergency Management
Marty Vanier, National Agricultural Biosecurity Center
Rich Vargo, Riley County Clerk's Office
Gayle Willard, Kansas State University
William Wilson, U.S. Department of Agriculture

MEETING 4
AGENDA

March 16, 2012
Keck Center of the National Academies
Washington, DC

9:00 a.m.	Registration
9:30 – 9:40 a.m.	Welcome and Opening Remarks *Greg Baecher (Chair)*
9:40 – 9:55 a.m.	Introductory Remarks *Tara O'Toole (DHS Under Secretary for Science and Technology)*
9:55 – 10:45 a.m.	Q&A Session by Committee *Moderated by Greg Baecher (Chair)*
10:45 – 10:50 a.m.	Break
10:50 – 11:30 a.m.	Q&A Session by Committee *Moderated by Greg Baecher (Chair)*
11:30 a.m. – noon	Public Comments Please register in advance
12:00 p.m.	Closing Remarks and Adjourn

MEETING 4
LIST OF PUBLIC PARTICIPANTS

George Bieberbach, National Center for Atmospheric Research
Paul Bieringer, STAR
Julie S. Brewer, U.S. Department of Homeland Security
Naeem Brewington, U.S. Department of Homeland Security
Ellen P. Carlin, Committee on Homeland Security, U.S. House of
    Representatives
Rocco Casagrande, Gryphon Scientific
Eugene Cole, Department of Homeland Security
Randall Crom, National Center for Animal Health Emergency
    Management
Kimberly Forde-Folle, U.S. Department of Agriculture

Myles Gardner, Signature Science
Cyril Gerard Gay, U.S. Department of Agriculture
Adam Hamilton, Signature Science
Natasha Hawkins, U.S. Department of Homeland Security
Molly Isbell, Signature Science
James Johnson, U.S. Department of Homeland Security
Steven Kappes, U.S. Department of Agriculture
Mark Kazmierczak, Gryphon Scientific
Christopher Kiley, Merrick and Company
Joseph Kozlovac, U.S. Department of Agriculture
Christopher Kronser, FLAD Architects
Elizabeth Lautner, U.S. Department of Agriculture
Michael Moreland, Perkins and Will
Mark Mussante, Gryphon Scientific
Tara O'Toole, U.S. Department of Homeland Security
Dustin Pendell, Colorado State University
Joel Piper, U.S. Department of Homeland Security
Sharla Rausch, U.S. Department of Homeland Security
Michael Robertson, U.S. Department of Homeland Security
Margaret Rush, Gryphon Scientific
Dana Shea, Congressional Research Service
Wayne Stoskopf, Office of Congresswoman Lynn Jenkins (R-KS)
Sara Szmania, Signature Science
John Verrico, U.S. Department of Homeland Security