




Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options

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Meeting Critical Laboratory Needs for Animal Agriculture

Examination of Three Options

Committee on an Analysis of the Requirements and
Alternatives for Foreign Animal and Zoonotic Disease
Research and Diagnostic Laboratory Capabilities

Board on Agriculture and Natural Resources

Board on Life Sciences

Division on Earth and Life Studies

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Preface

In April 2012, the National Research Council convened a committee to provide advice on the requirements and alternatives for ensuring the nation has the necessary foreign animal and zoonotic disease research and diagnostic laboratory capabilities. In less than three months after the first public meeting to gather information, held on the rather inauspicious date of Friday the 13th (of April), the committee produced this report that analyzes three options for meeting our nation's biocontainment facility needs. The committee developed a conceptual framework for an ideal system that would best capture the broad intellectual capital of the United States and would take strategic advantage of investments in laboratory infrastructure during the last decade. It was against this backdrop that the committee considered the three options. The first of three options specified in the committee's statement of task was to build the National Bio- and Agro-Defense Facility (NBAF) as currently designed. The committee also evaluated whether two alternative options could provide the needed capability and capacity for addressing disease threats. These two alternative options were to build an NBAF of reduced size and scope ("NBAF-lite," as the committee colloquially referred to it during discussions), and to maintain our current national biocontainment laboratory on Plum Island, with large-animal biosafety level 4 containment capacity provided by foreign laboratories.

A report of this nature and with our timeline does not happen without the commitment and dedicated efforts of many people. That commitment was not only to the task at hand but to a \$165 billion animal agricultural enterprise that could suffer catastrophic losses as a result of diseases that are among the world's most infectious and most virulent. The commitment also extended to a nation that is struggling with economic realities as formidable as any we have faced for 75 years, to a nation that correctly questions a billion-dollar investment in a new facility, and to a leadership that must make decisions about that investment. We trust that this report will be a valuable resource in helping to make critical decisions that affect the security of our food supply, the viability of our agriculture industry, and the public health of our country. The committee dedicated itself to this study with those overarching considerations always in mind.

Committee members brought a broad array of experience and expertise to the discussions. Each of them made valuable contributions to this report, and my thanks go to them for their extraordinary efforts. The National Research Council staff who supported the project were outstanding. Their contributions, both directly and behind the scenes, and their timely encouragement of the chair when there seemed to be no possible way to accomplish our task in the allotted time, were invaluable. I thank all of them on behalf of a grateful committee.

Terry McElwain, DVM, PhD, *Chair*
Committee on an Analysis of the
Requirements and Alternatives for Foreign
Animal and Zoonotic Disease Research and
Diagnostic Laboratory Capabilities

Acknowledgments

The committee is grateful to all those who participated in our public sessions and those who provided information about their laboratories.

This report has been reviewed in draft form by persons 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 the 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 of objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of the report:

Ivan Damnjanovic, *Texas A&M University*
John R. Henneman, *The Pennsylvania State University*
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at Galveston*
Derrell Peel, *Oklahoma State University*
James A. Roth, *Iowa State University*
Harry Snelson, *American Association of Swine Veterinarians*

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 the report was overseen by **Dr. May Berenbaum, University of**

Illinois at Urbana-Champaign, and Dr. Lynn Goldman, George Washington University. Appointed by the National Research Council, they were responsible for making certain that an independent examination of the report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of the report rests with the authoring committee and the institution.

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Acronyms and Abbreviations

AAHL	Australian Animal Health Laboratory
AAVLD	American Association of Veterinary Laboratory Diagnosticians
ABSL	animal biosafety level
AHRC	Animal Health Research Center
APHIS	USDA Animal and Plant Health Inspection Service
ASF	African swine fever
ARS	USDA Agricultural Research Service
BID ₅₀	50% bovine infectious dose
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BRI	Biosecurity Research Institute
BSE	bovine spongiform encephalopathy
BSL	biosafety level
CAHFS	California Animal Health and Food Safety
CDC	Centers for Disease Control and Prevention
CSF	classical swine fever
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CVB	Center for Veterinary Biologics
DHS	US Department of Homeland Security
DIVA	differentiating infected from vaccinated animals
EEDA	emerging and exotic diseases of animals
ELISA	enzyme-linked immunosorbent assay
FAD	foreign animal disease
FAD&E	foreign animal diseases and ectoparasites
FADD	foreign animal disease diagnostics
FADDL	Foreign Animal Disease Diagnostic Laboratory
FAO	Food and Agriculture Organization of the United Nations
FBI	Federal Bureau of Investigation
FDA	US Food and Drug Administration

FLI	Friedrich-Loeffler-Institut
FMDv	foot-and-mouth disease virus
FY	fiscal year
GNL	Galveston National Laboratory
HSADL	High Security Animal Disease Laboratory
HSPD	Homeland Security Presidential Directive
IAH	Institute for Animal Health
IRF	Integrated Research Facility
ITAD	international transboundary animal disease
IVI	Institute of Virology and Immunoprophylaxis
NADC	National Animal Disease Center
NAHLN	National Animal Health Laboratory Network
NBACC	National Biodefense Analysis and Countermeasures Center
NBAF	National Bio- and Agro-Defense Facility
NBL	National Biocontainment Laboratory
NCAH	National Centers for Animal Health
NCFAD	National Centre for Foreign Animal Disease
NEIDL	National Emerging Infectious Diseases Laboratory
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NVSL	National Veterinary Services Laboratories
O&M	operations and maintenance
OIE	World Organisation for Animal Health
PAAR	Plant Animal Agrosecurity Research
PANAFTOSA	Pan-American Foot-and-Mouth Disease Center
PCR	polymerase chain reaction
PGP	percentage of protection against generalized foot infection
PIADC	Plum Island Animal Disease Center
PPE	personal protective equipment
RBL	Regional Biocontainment Laboratory
RCE	Regional Center of Excellence for Biodefense and Emerging Infectious Diseases
RML	Rocky Mountain Laboratories
SARS	severe acute respiratory syndrome
SEPRL	Southeast Poultry Research Laboratory
TAD	transboundary animal diseases
TB-LAM	tuberculosis-lipoarabinomannan
USAMRIID	US Army Medical Research Institute for Infectious Diseases
USDA	US Department of Agriculture
VSTA	Virus Serum Toxin Act

Summary

In 2006, the Department of Homeland Security (DHS) proposed creating the National Bio- and Agro-Defense Facility (NBAF) under the provisions of Homeland Security Presidential Directive 9, which allows DHS to expand its efforts to protect US agriculture and public health. The NBAF was envisioned to have the capacity and capability to conduct research and diagnostic activities for foreign animal diseases (FADs) and zoonotic diseases (diseases that are transmissible between animals and humans) at high-biocontainment levels¹ that can accommodate livestock species. It was also intended to replace the aging Plum Island Animal Disease Center (PIADC), which for more than 50 years has been part of the federal network of laboratories in which research and diagnostics on FADs are conducted. PIADC is the only US facility authorized to conduct research on foot-and-mouth disease, a highly contagious disease that the United States has been free of since 1929 and that constitutes a major threat to the US livestock industry.

US animal agriculture is valued at \$165 billion and is a principal source of food, a major source of livelihood for Americans, and a major contributor to US agricultural exports. Given its importance, there is a need to protect it from threats of FADs and zoonotic diseases and from potential threats caused by new and emerging pathogens. The proposed NBAF has been envisioned as a next-generation laboratory that would have a central role in the national infrastructure needed to handle threats from FADs, zoonotic diseases, and emerging diseases. However, construction of the proposed NBAF will incur a large expense. With the estimated cost of \$1.14 billion to construct the NBAF at the proposed site and the country's current fiscal challenges, DHS turned to the National Research Council for expert advice to assess the disease threats to US animal and public health, describe the laboratory capabilities and capacity needed to address those threats, and analyze three proposed options to meet laboratory needs. The three options as stipulated by DHS are (1) constructing the NBAF as designed, (2) constructing a scaled-back version of the NBAF to be described by the commit-

¹High biocontainment is used in the report to refer to biosafety levels (BSL) 3 or 4. A description of biosafety levels is found in Box 3-1.

tee, and (3) maintaining current capabilities at PIADC while leveraging ABSL-4 laboratory capacity (for livestock) by using foreign laboratories.

In response to the request, the National Research Council convened an ad hoc committee to conduct a scientific assessment of the requirements for a foreign animal and zoonotic disease research and diagnostic laboratory facility in the United States. As part of its task, the committee assessed the threats to US livestock from current and emerging diseases, including zoonoses, considered an ideal system for addressing those disease threats, and identified the laboratory infrastructure in which the diseases could be diagnosed and studied. The scope of the committee's analysis was limited to examining the three proposed options. The task explicitly excluded an assessment of specific site locations for the proposed laboratory facility; therefore, it was not within the committee's charge to compare the relative risks of the three options nor to determine where foot-and-mouth disease research can be safely conducted. The committee's conclusions and recommendation are summarized in Box S-1 at the end of this chapter.

IMPORTANCE AND VULNERABILITY OF US ANIMAL AGRICULTURE

The United States has been fortunate to have an abundance of natural resources to support its agricultural industry. But the continued success of the food-animal sector has also been due both to unparalleled advances in research that have resulted in remarkable gains in agricultural productivity, and to progress in eliminating many livestock and poultry diseases that still impact animal production and trade in other countries. Investments in an effective animal-health infrastructure have enabled US animal agriculture to focus on producing animals for food to meet growing domestic and international demands. However, the security of this multibillion-dollar enterprise and of the food system to which animal agriculture is intricately connected remains vulnerable to diseases threats, whether intentionally or naturally introduced.

Numerous recent National Research Council studies have assessed disease threats to animal and public health, and the committee did not attempt an exhaustive reconsideration of the broad array of disease agents that can affect animal agriculture. The list of disease threats has not changed nor have the drivers of disease emergence in our global society that can give rise to novel agents or to disease outbreaks caused by agents that are exotic to the United States. Animal diseases that have high priority with the US Department of Agriculture (USDA) also appear on the World Organisation for Animal Health (OIE) list of animal diseases; although many of these diseases are considered threats to livestock, many are also important zoonoses. In addition to naturally introduced disease threats, the nation also faces the threat of bio- or agroterrorism in which a disease agent is deliberately introduced to destabilize food sources or generate fear. Several homeland security presidential directives have focused on con-

fronting those potential hazards. Therefore, a comprehensive system to counter disease threats to animal agriculture is vital.

Recent epidemics of bovine spongiform encephalopathy (BSE) and foot-and-mouth disease in the United Kingdom, foot-and-mouth disease in South Korea and Taiwan, and highly pathogenic avian influenza A(H5N1) in Asia provide salient examples of the magnitude and breadth of possible consequences associated with disease outbreaks. The global severe acute respiratory syndrome (SARS) epidemic in 2003 demonstrates the effects of a disease that originated in animals and resulted in severe losses to individuals and many business sectors. Thus, whether they directly affect the health of animals only or whether they are transmitted from animals to humans, disease outbreaks have a major impact on agriculture, food security, and socioeconomic well-being.

THE ROLE OF A NATIONAL LABORATORY FACILITY IN AN INTEGRATED SYSTEM

Protecting US animal agriculture requires an integrated system that spans authorities, geography, and many programs and activities. The adage that a chain is only as strong as its weakest link applies to the complex systems needed to protect animal agriculture from the incursion of serious diseases and to address a riskier world. The committee addressed its study task in the context of an ideal integrated system for addressing FAD and zoonotic disease threats to the United States and considered what the role of a national biocontainment laboratory would be within such a system. The ideal system would capture and integrate the substantial human and physical assets distributed throughout the nation to address the threat of FADs and zoonotic diseases. It would include components of surveillance, diagnostics, and disease response and recovery. Research and development and workforce training are also critical core elements that support each of the functional arms (Figure S-1).

A national role in the coordination of the system is essential, and a federal laboratory or network of laboratories would be the cornerstone of an integrated system. The ideal system also reaches beyond national borders to tap the expertise and resources of the global infectious disease surveillance, diagnostic, and research communities. Recognizing the threat posed by zoonotic diseases and the known and potential roles that animals play in maintaining and transmitting infectious agents, the ideal system captures both human- and animal-health expertise and laboratory infrastructure to achieve common goals for disease recognition and response.

A substantial number of high-biocontainment (BSL-3 and BSL-4) laboratories have been constructed in the United States by federal and state agencies, universities, and private companies in the past 10 years. They provide an opportunity for collaborations that maximize national efforts to detect and respond to any incursion of an FAD or zoonotic disease. Strategic collaborations with other biocontainment facilities would also potentially enhance the efficient use of a

central laboratory. One example is the 13 regional BSL-3 containment laboratories constructed with funding from the National Institutes of Health (NIH). They are generally large facilities that include laboratory space for both *in vitro* and *in vivo* research and product-development activities to address emerging infectious diseases and pathogens of bioterrorism concern. Their activity focuses on pathogens of human-health importance, some of which may also affect agriculturally important animals.

BSL-4 laboratories with the capacity to handle large animals (ABSL-4 large animal) exist outside the United States. Each of them has the capability to handle livestock species and, depending on the situation at the time a request is made, may be willing to collaborate with US scientists to investigate pathogens that require ABSL-4 large-animal containment. However, the primary responsibility of those laboratories is to address their own national government and domestic needs.



FIGURE S-1 Components of an integrated national system for addressing foreign animal disease and zoonotic disease threats. Laboratory infrastructure underlies all components.

Although there are several BSL-4 laboratories in the United States, there is no ABSL-4 large-animal facility and the challenges of using the highest level of biocontainment space (ABSL-4) for large-animal research and diagnostic development are substantial. Additionally, the facilities at PIADC dedicated to FADs are dated and increasingly cost-inefficient. While biosafety level 3 agriculture (BSL-3Ag) containment space that is appropriate for research using group-housed agricultural animals has expanded through construction of several new facilities (such as the Biosecurity Research Institute and the National Animal Disease Center), it is insufficient to meet all of the needs for FAD research in

SUMMARY

5

the United States. Thus, there is a critical national need for laboratory capacity with modern BSL-3Ag and ABSL-4 large-animal capabilities that can serve as the hub of a national strategy for detection of and response to any incursion of an FAD and that can accommodate the study of infectious diseases of public-health importance in which livestock serve as key reservoir hosts. However, with the rapidly evolving nature of disease threats that confront animal health and with the rapid development of technologies for detecting and responding to diseases, planning for the construction of such a facility requires a flexible and nimble strategy for programmatic and facility design. Such a facility cannot stand alone and needs to be integrated in a national system. US programs for FAD and zoonotic disease detection and response (programs proposed for the NBAF) should have interfaces with similar activities and programs of the National Biodefense Analysis and Countermeasures Center, Centers for Disease Control and Prevention, the US Army Medical Research Institute for Infectious Diseases, USDA, NIH, and academic and state institutions to maximize efficiency and the use of intellectual resources through interdisciplinary research that crosses traditional agency boundaries. Such interagency working relationships would be essential for maximizing the success of the NBAF.

ANALYSIS OF THREE LABORATORY INFRASTRUCTURE OPTIONS

Laboratory infrastructure underlies all components of an ideal integrated system to address disease threats. Such a laboratory infrastructure would include the capacity to safely perform diagnostics, to conduct research on foot-and-mouth disease, to conduct research on non-foot-and-mouth disease FADs and zoonotic diseases in BSL-3Ag facilities, to undertake special pathogen activities in BSL-4 and ABSL-4 facilities, to support teaching and training, and to enable vaccine or other product development. In the context of these critical core laboratory components, the committee examined the advantages and liabilities of the three proposed options in its statement of task: constructing NBAF as currently designed, scaling back the size and scope of the proposed NBAF, or maintaining the current PIADC and leveraging the US capability and capacity through international laboratories with ABSL-4 large-animal containment space.

Option 1, the NBAF as currently designed, includes all components of the ideal laboratory infrastructure in a single location and has been designed to meet the current and anticipated future mission needs of DHS, the USDA Agricultural Research Service (ARS), and the USDA Animal and Plant Health Inspection Service (APHIS). It creates ABSL-4 large-animal capacity and additional BSL-3Ag capacity in the United States and would provide the United States with needed in-country infrastructure to address FAD and zoonotic disease threats. By housing the laboratory components in one facility, it avoids a need to move specimens or materials (some of which may be select agents) from other facilities and avoids a need to rely on partner entities in the United States or internationally. However, there are also drawbacks. Substantial costs are associated

with the construction, operation, and management of the proposed NBAF in addition to costs associated with the proposed expansions in DHS, USDA-ARS, and USDA-APHIS programs. Because it houses the laboratory components and associated research, development, and training activities in a central facility, the proposed NBAF does not fully utilize other existing and complementary investments in high-biocontainment laboratory, diagnostic, training, and vaccine development capacity in the United States and has the potential for duplication of resources—duplication that could be addressed by exploring partnerships with other facilities.

Several components of the NBAF as currently designed could potentially be reduced in size and scope or eliminated if US and international partnerships were used to meet the needs of an ideal system. In analyzing Option 2, an NBAF of reduced size and scope as described by the committee, examples of the areas that the committee suggested could be considered for reduction or elimination from the proposed NBAF are the biodevelopment module (BDM) for pilot vaccine production and BSL-3Ag rooms designated for training along with the associated training necropsy room. The committee also suggested that reductions in the sizes of the BSL-3Ag animal rooms, the ABSL-4 small-animal rooms, and the associated BSL-3E and BSL-4 laboratory space could be considered. The pilot vaccine production work conducted in the BDM, which is outside the biocontainment envelope, and most teaching and training activities could be conducted in collaboration with other US federal, state, university, and private-sector laboratories. Option 2 would have lower construction costs than the proposed NBAF and might also have lower sustained operations costs, although the actual cost implications are not clear given the limited and insufficient information provided by DHS. The NBAF of reduced size and scope as described by the committee would still consolidate DHS, USDA-ARS, and USDA-APHIS missions in a single location and address critical core gaps in BSL-3Ag and ABSL-4 large-animal capabilities in the United States. It could also make more efficient use of recently expanded US high-biocontainment laboratory capacity while achieving the overall needs of countering FAD and zoonotic disease threats to the nation. Option 2 highlights a change in the approach to animal diseases by drawing on scientific and research expertise available in other federal laboratories and outside government, providing intellectual benefits and possible cost savings through increased efficiencies by avoiding duplication, and fostering greater collaboration between researchers as part of an integrated US system for countering FAD and zoonotic disease threats. Finally, by relying on a network of partners, this option may provide increased flexibility to re-evaluate laboratory infrastructure needs periodically in light of new and emerging disease priorities and technologies. In contrast, not all components of the ideal system would be housed in a single facility. Implementing this option successfully would require the creation of agreements with the necessary federal agency and nongovernment partner facilities, including funding commitments to partner facilities to conduct collaborative work and management capacity to oversee collaborations. Pursuing this option would thus have policy implications and

SUMMARY

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might require DHS and USDA to make priority-setting decisions, given the potential reductions in designated agency laboratory space in the central facility.

A partnership of a central national laboratory of reduced scope and size and a distributed laboratory network can effectively protect the United States from FADs and zoonotic diseases, potentially realize cost savings, reduce redundancies while increasing efficiencies, and enhance the cohesiveness of a national system of biocontainment laboratories. However, because the cost implications of reducing the scope and capacity of a central facility cannot be known without further information and study, it will be important for DHS and USDA to make a good-faith effort to re-examine construction and operating costs of a laboratory of reduced size and complexity, and to also consider what those implications are for priority-setting decisions.

Option 3, maintaining PIADC and leveraging ABSL-4 large-animal capacity through other partners, would utilize an existing US facility that provides some of the needed laboratory infrastructure components and would avoid the costs of constructing a new replacement facility. PIADC is also the only US facility for research, diagnostics, and training related to foot-and-mouth disease. However, DHS highlighted the fact that the facilities at PIADC are aging and do not meet current standards for high-biocontainment laboratories. There are substantial costs associated with maintaining and operating PIADC over the long term, it lacks BSL-4 and ABSL-4 capabilities, and the committee was informed by DHS that such facilities could not be constructed at PIADC. If a full commitment were made to improving and maintaining PIADC, a period of transition to a new facility with a window of potential loss of function would not be needed. Option 3 would also realize the benefits of capital renovations and improvements that must be made no matter which option is selected over a longer period. As the committee explored the potential of relying on international partners for emergency work that might require ABSL-4 large-animal laboratory space, it found remarkably little capacity near the United States. Because this option would not provide the United States with ABSL-4 large-animal capabilities, agreements with foreign partners for access to ABSL-4 large-animal space and funding to support these collaborations would be required. Although that could enhance international collaboration in research on FADs and zoonotic diseases, it could limit the availability of ABSL-4 capabilities in a time of critical need, depending on the priorities of the foreign countries, and would separate ABSL-4 large-animal facilities from other FAD research.

ESSENTIAL CAPABILITIES NEEDED

Research to understand and protect the United States from the consequences of an outbreak of foot-and-mouth disease remains a high priority, and PIADC is the only US facility currently authorized to conduct work with foot-and-mouth disease virus (FMDv). Because foot-and-mouth disease research remains critical for the US animal-health system, the committee concludes that it will be essen-

tial to support PIADC until an alternative facility is authorized, constructed, commissioned, and approved for work with FMDv.

Although current livestock-specific FADs do not require BSL-4 laboratory containment, a disease outbreak caused in US livestock by a highly contagious zoonotic virus or a novel pathogen of undetermined transmissibility would require appropriate emergency biocontainment; it would also require research in live animals to characterize the infectious agent, transmission, and host range and susceptibility and to validate diagnostics. The committee notes that it is in the interest of the United States to pursue partnerships with countries that have ABSL-4 large-animal laboratories for the study of zoonotic agents of agricultural concern. However, given the uncertainty of priorities of a foreign laboratory and logistical difficulties in an emergency, it would not be desirable for the United States to rely on international laboratories to meet ABSL-4 large-animal needs in the long term. Therefore, as part of the national infrastructure for protecting animal and public health, the committee concludes that there is an imperative to build ABSL-4 large-animal space in the United States.

CONSIDERATIONS FOR FULFILLING NATIONAL NEEDS

Realizing cost savings in the construction and operation of laboratory facilities is a critically important objective; however, it is no less important for DHS, USDA, and other relevant agencies to maintain their focus on the overarching goal of developing a highly capable system for addressing FAD and zoonotic disease threats. A central laboratory would be a key part of an integrated national system, but it would only be one component of the system; therefore, the committee concludes that innovative, forward-thinking solutions are required not only about the central laboratory but about the entire system. The solutions for the entire system may need to involve consideration of a wider range of options for the central laboratory. That analysis extends beyond the scope of the current study.

In exploring national capabilities, the committee found a substantial number of public and private biocontainment laboratories across the country; these are capabilities that did not exist nearly a decade ago when Homeland Security Presidential Directive 9 was issued, nor did they exist when previous NRC reports on options for a national biocontainment laboratory were issued. Institutions that house a variety of BSL-3, BSL-3Ag, and BSL-4 laboratories in the United States can serve as partners in a national system and those existing capabilities can be leveraged in the national interest. The major barriers to leveraging capabilities at those facilities are the need to establish formal relationships, agreed-upon operational protocols, contractual funding arrangements, and well-reasoned policies about the kind of work that can be conducted in different facilities. Yet in the committee's view, it is precisely those kinds of relationships that could move the nation closer to the ideal, integrated national system to address animal disease threats—one in which a distributed laboratory network is

tied closely to a central supporting facility. **Regardless of the options considered for a central facility, the committee recommends that DHS and USDA develop and implement an integrated national strategy that utilizes a distributed system for addressing FAD and zoonotic disease threats.** The National Animal Health Laboratory Network is an excellent model of such a distributed laboratory network and would serve a critical role in a more comprehensive and integrated national strategy.

Balanced Support for Infrastructure and Research and Development

The committee concludes that it is critical for policy-makers and agency planners to recognize that an effective system for addressing FAD and zoonotic disease threats to the United States consists of more than facilities; it also requires robust research programs. Those cannot be traded off against one another; rather, balanced support is needed to enable the continuation of research priorities and capital costs associated with maintaining or constructing modern laboratory facilities.

Ongoing Planning and Prioritizing for the National System

The committee concludes that conceptualizing, implementing, and maintaining a US national system to address threats posed by FADs and zoonotic diseases requires not only an understanding of today's priorities and technologies but continued monitoring and assessment to understand how the high-priority threats and the tools available to address them change over time. Such vision and planning are critical and must be ongoing. There is a related need for continuing communication and coordination among the many parties and stakeholders that form an efficient, effective, and integrated national system.

Alternative Funding Mechanisms

The committee concludes that exploring alternative funding mechanisms to supplement current federal allocations for capital and operational costs and for program support would be useful. Alternative funding strategies used by other countries could be considered as possible models. For instance, Australia draws on industry contributions to help support its national animal disease capabilities. It may also be useful to explore the possibility of using public-private partnerships to support and maintain aspects of facilities and research programs.

Consideration of All Factors of Concern

The importance of having a strong national system to recognize and counter the threats posed by FADs and zoonotic diseases may not always be apparent when disease outbreaks are quickly identified, mitigated, and contained, but the consequences of such disease outbreaks can be enormous if and when a system fails. This study provides a high-level view of whether each of the three options stipulated by DHS could be feasible in meeting the nation's needs. As discussed in Chapter 4, the committee also recognizes that the three DHS-proposed options may not be the only options worth considering. Concerns considered in this study—costs, necessary capabilities, and infrastructure needs—do not reflect all of the factors decision-makers must consider. The factors that were considered in the original assessment that led to decisions about the NBAF may or may not have changed. For example, safety concerns still linger on the issue of bringing foot-and-mouth disease research onto the US mainland and the risk of accidental release of FMDv and its consequent impacts. Decisions about infrastructure needs should not be made in the absence of risk concerns as well as the many other factors worthy of consideration. The committee concludes that to most appropriately fill critical laboratory needs in the United States, all factors of concern (including site location, risk assessment, political considerations, adaptability for the future) will need to be considered in a more comprehensive assessment.

BOX S-1

Conclusions and Recommendation for Meeting Critical Laboratory Needs

It is imperative to establish research, diagnostic, and surveillance laboratory capabilities commensurate with the size and value of the US animal agriculture industry to prevent or mitigate a disease outbreak that could have devastating effects on human and animal lives and livelihoods. The ideal system to counter threats from foreign animal diseases (FADs) and zoonotic diseases includes research, development, and training; a centralized core facility; a distributed network of national and international partnerships; and disease surveillance, diagnostic, and response capabilities. A central laboratory would be a key part of an integrated national system, but it would only be one component of the system. In addressing its Statement of Task, the committee provides the following conclusions and recommendation for fulfilling critical laboratory needs in the United States.

CONCLUSIONS

Conclusion 1: The National Bio- and Agro-Defense Facility (NBAF) as currently designed includes all components of the ideal laboratory infrastructure in a single location and has been designed to meet the current and anticipated future

(Continued)

BOX S-1 Continued

mission needs of the Department of Homeland Security (DHS), the US Department of Agriculture (USDA) Agricultural Research Service (ARS), and the USDA Animal and Plant Health Inspection Service (APHIS); but the proposed facility also has drawbacks (i.e., substantial costs associated with construction, operation, and management; not leveraging existing capacity and potential duplication of resources).

Conclusion 2: A partnership of a central national laboratory of reduced scope and size and a distributed laboratory network can effectively protect the United States from FADs and zoonotic diseases, potentially realize cost savings, reduce redundancies while increasing efficiencies, and enhance the cohesiveness of a national system of biocontainment laboratories. However, given the limited and insufficient information provided by DHS, the cost implications of reducing the scope and capacity of a central facility cannot be known without further information and study.

Conclusion 3: Maintaining the Plum Island Animal Disease Center (PIADC) and drawing on the ABSL-4 large-animal capacity of other partners would utilize an existing US facility that provides some of the needed laboratory infrastructure components and would avoid the costs of constructing a new replacement facility. However, the facilities at PIADC are aging and do not meet current standards for high-biocontainment laboratories. There are substantial costs associated with maintaining and operating PIADC over the long term, it lacks BSL-4 and ABSL-4 large-animal capabilities, and the committee was informed by DHS that such facilities could not be constructed at PIADC. Given the uncertainty over priorities of a foreign laboratory and logistical difficulties in an emergency, it would not be desirable for the United States to rely on international laboratories to meet ABSL-4 large-animal needs in the long term.

Conclusion 4: Because foot-and-mouth disease research remains critical for the US animal-health system, it will be essential to support PIADC until an alternative facility is authorized, constructed, commissioned, and approved for work with FMDv.

Conclusion 5: As part of the national infrastructure for protecting animal and public health, there is an imperative to build ABSL-4 large-animal space in the United States.

Conclusion 6: Innovative, forward-thinking solutions are required not only about the central laboratory but about the entire system.

Conclusion 7: It is critical for policy-makers and agency planners to recognize that an effective system for addressing FAD and zoonotic disease threats to the United States consists of more than facilities; it also requires robust research programs.

Conclusion 8: Conceptualizing, implementing, and maintaining a US national system to address threats posed by FADs and zoonotic diseases requires not only an understanding of today's priorities and technologies but continued monitoring and assessment to understand how the high-priority threats and the tools available to address them change over time. Such vision and planning are critical and must be ongoing.

Conclusion 9: Exploring alternative funding mechanisms to supplement current federal allocations for capital and operational costs and for program support would be useful.

(Continued)

BOX S-1 Continued

Conclusion 10: To most appropriately fill critical laboratory needs in the United States, all factors of concern (including site location, risk assessment, political considerations, adaptability for the future) will need to be considered in a more comprehensive assessment.

RECOMMENDATION

Regardless of the options considered for a central facility, the committee recommends that DHS and USDA develop and implement an integrated national strategy that utilizes a distributed system for addressing FAD and zoonotic disease threats.

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Introduction

BACKGROUND

In 2004, President George W. Bush issued Homeland Security Presidential Directive 9 (HSPD-9),¹ which “establishes a national policy to defend the agriculture and food system against terrorist attacks, major disasters, and other emergencies.” Among the key provisions of HSPD-9, the Secretaries of Agriculture and Homeland Security are called on to coordinate a federal effort to “expand development of current and new countermeasures against the intentional introduction or natural occurrence of catastrophic animal, plant, and zoonotic diseases.” This coordinated effort would address research and development related to new methods of detecting, diagnosing, and preventing foreign animal diseases (FADs)² and zoonotic diseases.³ Such research and development activities would require “safe, secure, and state-of-the-art agriculture biocontainment laboratories” to conduct such work.

The United States currently has a network of federal, state, and university-based laboratories that conduct research and diagnostic activities on animal diseases. The laboratory network includes the Plum Island Animal Disease Center (PIADC), a federally-owned and operated facility on Plum Island, off the coast of Long Island, New York. PIADC is the only laboratory in the United States in which foot-and-mouth disease virus can be studied; foot-and-mouth disease is a highly contagious FAD that affects cloven-hoofed animals and has potentially catastrophic agricultural and economic consequences. The United States has been free of foot-and-mouth disease since 1929. For more than 50 years, PIADC has conducted research and diagnostic activities on foot-and-mouth disease and other foreign animal diseases. Similar research on the most highly contagious

¹Available online at http://www.aphis.usda.gov/animal_health/emergency_management/downloads/hspd-9.pdf (accessed May 30, 2012).

²Foreign animal diseases are caused by animal disease agents that do not occur naturally in the United States and that affect agriculturally important animals (NRC, 2005).

³Zoonotic disease agents can be transmitted between animals and humans (IOM and NRC, 2009).

zoonotic agents that also infect livestock species has not been conducted at PIADC, because of its focus on the highest-priority animal diseases (such as foot-and-mouth disease) and its lack of biosafety level 4 (BSL-4) containment areas, which are necessary for studying deadly zoonotic diseases that have no known treatment or cure. Examples of BSL-4 pathogens include Nipah and Hendra viruses.

HSPD-9 allows the Department of Homeland Security (DHS) to expand its efforts in protecting the country against intentional or natural occurrences of FADs and zoonotic diseases. The aging facilities at PIADC and the lack of BSL-4 capacity prompted DHS to propose the creation of a National Bio- and Agro-Defense Facility (NBAF) in 2006. The proposed facility is designed to replace PIADC. It would carry out the current mission of PIADC and expand that mission to include the study of zoonotic diseases in BSL-4 and in animal biosafety level 4 (ABSL-4) large-animal containment for accommodating livestock species.

According to DHS, the NBAF would provide “capabilities to perform basic and advanced research; enhanced means to perform laboratory diagnostic detection and response; expanded capabilities for development of new vaccines against high-threat foreign animal diseases; and facilities for training veterinarians in preparedness and response to high-consequence foreign animal disease outbreaks” (DHS, 2012, pp. ES-2-ES-3). DHS now estimates that it would cost \$1.14 billion to construct the NBAF in Manhattan, Kansas.⁴

THE COMMITTEE’S TASK

Given the estimated cost of constructing the proposed NBAF and the country’s current fiscal challenges, DHS requested that the National Research Council assess the disease threats to US animal and public health, describe the laboratory capabilities needed to address the threats, and analyze three proposed options to meet those needs. The three options as stipulated by DHS are (1) constructing the NBAF as designed, (2) constructing a scaled-back version of the NBAF, and (3) maintaining current capabilities at PIADC and leveraging BSL-4 laboratory capacity (for livestock) by using foreign laboratories. The statement of task is provided in Box 1-1.

The National Research Council convened an ad hoc committee to conduct a scientific assessment of the requirements for an FAD and zoonotic disease research and diagnostic laboratory facility in the United States (see Appendix A for committee biosketches). The committee members have expertise in animal diseases, animal health, zoonotic disease threats to public health, the livestock industry, national security aspects of agriculture, agricultural economics, biosafety, biosecurity, and laboratory biocontainment.

⁴Estimate provided in the opening remarks to the committee by Tara O’Toole, US Department of Homeland Security Under Secretary for Science and Technology. Opening remarks were given at the committee meeting held on April 13, 2012, in Washington, DC.

BOX 1-1
Statement of Task

A committee of experts will conduct a scientific assessment of the requirements for a foreign animal and zoonotic disease research and diagnostic laboratory facility in the United States. Specifically, the committee will:

1. Assess the threat posed to livestock by infectious diseases, such as zoonoses, current and emerging diseases, and bioterrorist agents. For this effort, the committee will rely upon a literature review of relevant articles and reports addressing foreign animal diseases, agricultural bioterrorism, emerging and zoonotic diseases. DHS and USDA will provide relevant materials to assist the committee.
2. Identify the US laboratory and related infrastructure needed to counter the threat and meet the animal health, public health, and food security needs of the United States.
3. The committee will examine alternative approaches to providing the needed infrastructure, focusing on three options:
 - Building the NBAF as currently designed;
 - Building a scaled-back version of the NBAF (to be described by NRC/NAS);
 - Maintaining current capabilities at PIADC while leveraging BSL-4 laboratory capacity (for livestock) through foreign laboratories.

In evaluating alternatives, the committee will examine factors such as capacity and capabilities, advantages and liabilities, relative costs, and other considerations in relation to the mission needs of DHS and USDA (Agricultural Research Service and Animal and Plant Health Inspection Service) to counter the known and emerging threats from bioterrorism, foreign animal diseases and zoonotic diseases.

The committee's report will identify pros and cons, discuss potential gaps, and provide consensus advice on how the laboratory infrastructure needed to address emerging foreign animal and zoonotic disease threats could be assembled.

The committee's examination will address the capability needed to counter the identified threat, relative to the three options. The committee will not consider specific site locations as part of this examination.

The Committee's Approach to Its Task

The committee was given three months to complete its task. As part of its information-gathering activities, the committee held its first meeting on April 12-14, 2012, in Washington, DC. At the meeting, representatives of DHS and the US Department of Agriculture (USDA) briefed the committee on their rationale and expectations for the study, and DHS indicated that it intended to use the findings and conclusions of the committee's report to inform its decision-making process. DHS and USDA discussed the scientific programs at PIADC and those planned for the NBAF and briefed the committee on the current infrastructure and operating costs of PIADC and on the mission requirements, build-

ing designs, and construction costs of the proposed NBAF in Manhattan, Kansas.

The committee invited outside experts to speak about the capabilities and capacities of laboratories that would be similar to the NBAF. These included the Biosecurity Research Institute at Kansas State University in Manhattan, Kansas; the Centers for Disease Control and Prevention in Atlanta, Georgia; the National Centre for Foreign Animal Disease in Winnipeg, Canada; the Friedrich-Loeffler-Institut in Insel Riems, Germany; and the Australian Animal Health Laboratory in East Geelong, Victoria, Australia (see Appendix B for meeting agendas).

In gathering additional information about current US capabilities and infrastructure for handling FADs and zoonotic diseases, the committee arranged public teleconferences with the directors of three additional laboratories in the United States: the National Biodefense Analysis and Countermeasures Center of DHS, the US Army Medical Research Institute for Infectious Diseases, and the Rocky Mountain Laboratories of the National Institute of Allergy and Infectious Diseases (see Appendix B for the teleconference agendas). The committee also discussed the capabilities and capacities of representative regional laboratories.

The second committee meeting was held on May 22-23, 2012, in Irvine, California, and was closed to the public in its entirety. The purpose of the meeting was to finalize the committee's findings and conclusions and prepare its report for external peer review.

Limitations of the Scope of the Committee's Task

As part of its task, the committee assessed the threats to US livestock by current and emerging diseases, including zoonoses, and identified the specific requirements for a high-biocontainment laboratory where these diseases could be diagnosed and studied. The scope of the committee's analysis was limited to examining the three proposed options and whether each would have the capability of adequately addressing the current and future needs for conducting research and diagnostic activities related to FAD and zoonotic disease threats. Although the committee was required to focus its analysis on the three proposed options, it acknowledges that other viable options are available but it was prohibited from providing an in-depth analysis of the feasibility of other alternatives in this report.

The statement of task also explicitly prohibits the committee from considering specific site locations as part of its examination of the three options. Although the committee was asked to provide a comparison of the three options, it was beyond the committee's charge to compare risks between the proposed NBAF in Manhattan, Kansas (on the US mainland) and the PIADC on Plum Island, New York (off the coast). Whether foot-and-mouth disease research can be safely conducted on the US mainland is an issue of considerable debate (GAO, 2008, 2009). A separate National Research Council committee recently

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evaluated the adequacy and validity of an updated DHS site-specific risk assessment of the NBAF in Manhattan, Kansas. That committee concluded that the updated risk assessment was “technically inadequate in critical respects” and that it remains “an insufficient basis on which to judge the risks associated with the proposed NBAF in Manhattan, Kansas” (NRC, 2012). In providing an analysis of the three proposed options in this report, it is beyond the scope of this committee’s task to discuss or provide judgment on whether foot-and-mouth disease research can be safely conducted on the mainland or where such research should take place.

The committee examined general design specifications as related to the research and diagnostic capabilities of the NBAF as currently proposed. The committee was asked to examine the NBAF as currently designed and to examine a scaled-back alternative, but it was beyond the committee’s task to conduct a detailed building design review or cost analysis.

ORGANIZATION OF THE REPORT

The report is composed of five chapters. Chapter 2 provides an overview of the threats posed by infectious diseases to US agriculture and human health. Chapter 3 describes an ideal system for addressing FADs and zoonotic diseases, the role of a central laboratory facility (such as an NBAF-type of laboratory) in a national system, and current capacity and capabilities and future needs for addressing FADs and zoonotic diseases in the United States. Chapter 4 analyzes the proposed options and discusses whether they provide the necessary infrastructure for effectively protecting animal health, public health, and food security against FAD and zoonotic disease threats in the United States. The committee elaborates on its conclusions and recommendation in Chapter 5.

REFERENCES

- DHS (US Department of Homeland Security). 2012. NBAF Updated Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment. Final Report, Vol. 1, February 2012 [online]. Available: http://www.dhs.gov/xlibrary/assets/st/nbaf_updated_ssra_volume_i.pdf (accessed May 30, 2012).
- GAO (US Government Accountability Office). 2008. High-Containment Biosafety Laboratories: DHS lacks evidence to conclude that foot-and-mouth disease research can be done safely on the U.S. mainland. Washington, DC: GAO [online]. Available: <http://www.gao.gov/products/GAO-08-821T> (accessed May 14, 2012).
- GAO. 2009. Observations on DHS’s Analyses Concerning Whether FMD Research Can Be Done as Safely on the Mainland as on Plum Island. Washington, DC: GAO [online]. Available: <http://www.gao.gov/products/GAO-09-747> (accessed May 14, 2012).
- IOM (Institute of Medicine) and NRC (National Research Council). 2009. Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases. G.T. Keusch, M. Pappaioanou, M.C. Gonzalez, K.A. Scott, and P. Tsai, eds. Washington, DC: The National Academies Press.

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National Research Council (NRC). 2005. *Animal Health at the Crossroads: Preventing, Detecting, and Diagnosing Animal Diseases*. Washington, DC: The National Academies Press.

NRC. 2012. *Evaluation of the Updated Site-Specific Risk Assessment for the National Bio- and Agro-Defense Facility in Manhattan, Kansas*. Washington, DC: The National Academies Press.

2

Critical Need to Protect US Animal Agriculture

IMPORTANCE OF ANIMAL AGRICULTURE

Value of and Demand for Animal Agriculture

Agriculture and food make up a major part of the US economy. In 2011, US farm cash receipts amounted to \$366 billion, of which about \$165 billion accrued was attributed directly to the livestock¹ sector (USDA-ERS, 2012a). Livestock and livestock-product exports amounted to \$26 billion in 2011, about 20% of total agricultural exports. In 2011, production agriculture accounted for about 1% of the US gross domestic product, total employment in agricultural and related industries was about \$2.3 million, and the net trade balance from the agricultural sector was about \$37 billion (USDA-ERS, 2012a). The crop sector depends heavily on feedstock demand from the domestic livestock production sector. The food sector is much larger: about 8.3 million people are employed in occupations related to food preparation and service (BLS, 2012a,b), and in 2010, US consumers spent about 9.4% of their disposable personal income on food (USDA-ERS, 2011). In 2012, US producers and ranchers are forecasted to produce 91.6 billion pounds of meat (beef, pork, lamb, chicken, and turkey); hens are projected to produce 6.62 billion dozen table eggs and 1.05 billion dozen hatching eggs; a US dairy cow is expected to produce an average of 21,825 pounds of milk; and US dairy cattle collectively are forecasted to produce 201.1 billion pounds of milk (USDA-ERS, 2012b).

The world population is expected to increase to 9.3 billion by 2050 (United Nations, 2011). With projected increases in global population and wealth and the resulting demographic changes that could lead to a burgeoning middle-class in developing countries, the demand for protein from animal sources will be

¹In this report, the term “livestock” refers to domestic animals such as cattle, swine, horses, sheep, and chickens that are raised on a farm for use or profit.

unprecedented, especially in developing countries, and will require a “livestock revolution” (Delgado et al., 1999). The Food and Agriculture Organization of the United Nations (FAO) estimates that feeding the world population in 2050 will require a 58% increase in meat production to produce a total of 470 million tons to meet the demand for animal protein (FAO, 2009), which would require exceptional growth in the production of animals and animal products.

Role of Research and Development in Animal Productivity

The United States has been fortunate in its abundance of natural resources to support agriculture, but recent success in the agricultural sector has been based on unparalleled advances in effective research that have resulted in remarkable gains in agricultural productivity. The ability to apply key research findings and technologies to enhancing the agricultural productivity has improved animal productivity and enabled farmers to produce more meat and milk products to meet growing demand while reducing resource use. For instance, increased animal productivity has enabled an increase in total milk production through increased production per cow even though the number of US dairy herds has decreased. The United States has also made progress in eliminating many of the livestock and poultry diseases that are still found in animal populations in other countries. However, there is concern about the future levels of investment in agricultural research and development that are required for continued scientific advances that can benefit US consumers and businesses and that can sustain our ability to be a global leader and producer.

US investment in an effective animal-health infrastructure, at both the state and national levels, has been instrumental in improving the health of our livestock and poultry populations and in protecting them against the incursion of foreign animal diseases (FADs) and the spread of endemic animal diseases. Through effective federal-state partnerships, animal-health officials continue to reduce and eliminate costly animal diseases, such as brucellosis, tuberculosis, pseudorabies, and exotic Newcastle disease. As a result, US producers have been able to focus on raising livestock and poultry with higher productivity values compared to those of other countries, where food animals are produced under the burden of diseases and parasites that greatly decrease their productivity, threaten public health through of zoonoses (diseases transmitted between humans and animals), and reduce food security.

Vulnerability of Animal Agriculture

US consumers have a stable, abundant, nutritious, and safe food supply. The stability of the food system is put at risk in part because of factors that drive the emergence of disease and disease vectors, and also due in part to factors that intensify and expand the interface between humans and animals and their prod-

ucts (IOM and NRC, 2009). Socioeconomic factors that affect disease emergence include increasingly globalized trade and changes in the environment that increase the movements of people, animals, and disease vectors (IOM and NRC, 2009). The movement of people, global travel and trade, the complexity of global food systems, and the ease with which pathogens circumnavigate the globe contribute to a significant threat to animal health and public health in that many animal diseases are also capable of infecting humans. Food animals are being produced in more concentrated and integrated systems, and this may also be a factor that could affect health and disease transmission.

Consequences of a Foreign Animal Disease or Zoonotic Disease Incursion

Disruptions in the food system could have catastrophic economic repercussions for US producers and for the systems and enterprises associated with animal agriculture. A major FAD or zoonotic disease event could result in economic losses of billions of dollars, including losses to producers, agricultural and food sector employees, consumers, and taxpayers; damages to landscape and environmental resources; and potential public-health costs associated with zoonotic diseases. Additional concerns include animal suffering, human psychological costs, and potential loss of public confidence. A large variety of significant losses may arise, depending in part on the event's location, on post-event management, and on international trade responses to the event. It is conceivable that large capital losses would materialize, as when many businesses in a region are forced to exit permanently. Recent experiences in the UK and elsewhere have dealt with bovine spongiform encephalopathy (BSE) and foot-and-mouth disease epidemics, which provide examples of the magnitude and breadth of possible consequences resulting from disease outbreaks.

Studies on the general matter have focused on foot-and-mouth disease, in part because this disease is of great concern and in part because several significant foot-and-mouth disease events have allowed modelers to better appreciate and formulate the more critical aspects of loss determinants. The 1997 foot-and-mouth disease outbreak in Taiwan undermined the viability of the island's pork production sector, which was heavily dependent on exports to Japan (Blayney et al., 2006). The UK experienced a severe foot-and-mouth disease outbreak in 2001 that lasted 221 days and resulted in 2,026 infected premises (UK-Defra, 2002). In controlling the foot-and-mouth disease outbreak, UK officials destroyed more than 6 million animals (including more than 1.2 million infected and more than 5 million healthy animals to prevent disease spread) at an estimated cost of US\$10.7-11.7 billion (Thompson et al., 2002) where the rural recreation sector also suffered large losses (Blake et al., 2003). In 2010, South Korea experienced its worst foot-and-mouth disease outbreak, which resulted in the culling of nearly 10 million swine and almost 3 million cattle and cost more than US\$1.8 billion (USDA-FAS, 2011).

Several economic studies have considered a foot-and-mouth disease outbreak in the United States. Ekboir (1999) estimated that the cost of a foot-and-mouth disease outbreak in the state of California alone would be \$8.5-13.5 billion, of which about \$6 billion would be attributed to an embargo on US meat exports. Paarlberg et al. (2002) estimated that a foot-and-mouth disease outbreak in the United States similar to the one that occurred in the UK in 2001 could generate US farm-income losses of \$14 billion. Zhao et al. (2006) considered a foot-and-mouth disease event of non-defined geographic origin and estimated total losses in the order of \$20 billion, or possibly much more if traceback is poor. The US bovine production and produce sectors are open and dispersed in form, and traceability for disease events has been problematic in the past. Carpenter et al. (2011) have integrated a spatial stochastic epidemic model into an economic analysis to conclude that a foot-and-mouth disease outbreak originating in a large California dairy herd could reasonably exceed \$20-30 billion in economic losses.

Other FADs and zoonotic diseases such as African swine fever, BSE, and highly pathogenic avian influenza could also result in large and varied losses. The global severe acute respiratory syndrome (SARS) epidemic in 2003 demonstrates the effects of a disease that originated in animals and resulted in severe losses to individuals and a large number of business sectors. Thus, whether they directly affect the health of animals only or whether they are transmitted from animals to humans, disease outbreaks have a major impact on agriculture, food security, and socioeconomic well-being.

CRITICAL INFRASTRUCTURE TO PROTECT ANIMAL HEALTH

The American public has come to expect a continuous, safe, and relatively inexpensive food supply. To maintain the status quo, it is critical for the United States to have an effective and integrated animal-health infrastructure in place that is commensurate with protecting an animal agriculture enterprise with annual revenues of \$165 billion (USDA-ERS, 2012a). Such an infrastructure is important for preventing the entry of FADs, rapidly detecting and responding to disease threats, implementing a response and recovery plan, training a workforce for routine and emergency situations, ensuring excellent diagnostic services, and maintaining an effective research and development program.

The recent economic recession and movements toward smaller government have resulted in a substantial reduction in the state and federal animal-health workforce and have decreased funding for research and diagnostics. At the same time, the Plum Island Animal Disease Center (PIADC)—the high-biocontainment laboratory that has served as a critical linchpin for safeguarding animal health by supporting diagnostics and research related to FADs—has continued to age well past its expected lifespan. The Department of Homeland Security (DHS) has determined that a new facility is necessary to replace the aging PIADC. However, in the current economic climate, DHS is facing a challenge in identifying

adequate resources to fund construction of a new laboratory as currently designed.

With that backdrop, new problems have emerged with respect to the commitment to and the resources necessary for addressing growing threats and for addressing the vulnerability of animal agriculture to FADs. The challenges have grown progressively more complicated with the shifting of the US financial and political landscape. The United States faces new realities for setting priorities, determining tradeoffs, and making key decisions.

The convergence of increased threats and consequences of animal disease epidemics, the need to have a diagnostic and research system commensurate with addressing the threats, and the reality of reduced resources to accomplish both have created four critical issues and decision points.

- First is the issue of reconciling the capital cost of a state-of-the-art laboratory for agricultural biodefense while investing in critical research. The need for both is clear, but providing funds for both may not be feasible.

- Second is the dilemma that centers on the need for continuing research and diagnostic capacity at the current facility while constructing and transitioning to a new facility. The expense of building one facility while maintaining another in order to maintain current capacity adds further budget pressure for 10-12 years.

- Third, the extended timeline from initial project approval through final construction and commissioning may be more than a decade, and this creates a dilemma in planning. Current disease threats may not be indicative of future disease threats, and the technological tools that are available for countering current disease threats may change rapidly over time and become outdated. That creates a challenge for ensuring that the new facility's capabilities and capacity are consistent with future needs and adaptable in the face of technological advances.

- Fourth, the present budget constraints that have led to the present committee's charge may persist. If they do, government programs and services that have received support in the past may need to be transformed and re-evaluated, and high-priority programs and facilities may need to be supported by alternative funding strategies. The latter requires innovative and strategic planning to make it possible to protect a national asset from FAD and zoonotic disease threats.

ANIMAL DISEASES OF CONCERN

In assessing the spectrum of livestock and poultry disease threats, the committee examined past high-priority diseases of concern to the US Department of Agriculture (USDA), current livestock and poultry notifiable-disease lists, the results of deliberations on disease threats that have occurred in recent years, and previous National Research Council reports. A broad array of diseases can be

considered threats to livestock and poultry, and many of them are also zoonoses of human health importance. The overlap among various studies and priority assessments is extensive. Most diseases that were previously identified as having high priority continue to remain a priority. Diseases that have newly emerged or that constitute threats because of potential intentional introduction have been added to the list of disease threats. Many threat-assessment studies have been conducted, but they typically have focused on specific disease types and used a wide variety of methods and so are not easily comparable. The committee was unaware of any threat assessments that used a common, quantitative, systematic, and comprehensive approach that would allow valid meta-analysis for setting priorities among disease threats. Integrating various components—such as transmission and spread models, economic effects, social effects, and effects on human and animal health—into a single assessment is difficult and has not typically been done. That gap in knowledge poses a serious challenge to systematic priority-setting among threats posed by diseases and has led to reliance on subject-matter experts for guidance on priorities for livestock and poultry disease threats on an ad hoc basis.

Diseases that have historically been considered by USDA to have the highest priorities for surveillance, vaccine research, and diagnostic test development have been infectious diseases of livestock and poultry that are exotic to the United States and endemic diseases that are regulated as a part of control and eradication programs, otherwise known as “program diseases”. The program diseases have included endemic diseases such as brucellosis, tuberculosis, pseudorabies, and avian influenza and FADs such as foot-and-mouth disease, classical swine fever (CSF), highly pathogenic avian influenza, and exotic Newcastle disease. In the last 15 years, of the 3,149 investigations that USDA conducted of possible FAD or emerging disease incidents, only a small percentage were confirmed as FADs or emerging diseases (USDA-APHIS, 2012). In 2011, USDA conducted 327 FAD investigations which resulted in only one confirmed FAD (USDA-APHIS, 2012).

The World Organisation for Animal Health (OIE) maintains a list of FADs and zoonotic diseases that can significantly impact animal populations and trade, and many of the same USDA program diseases appear on the OIE list. Since 2001, the threat of biological terrorism has focused on the intentional introduction of animal diseases, and there is substantial overlap among the threat agents identified (see section on “Agroterrorism” later in this chapter). These disease agents are also considered select agents and are listed in the National Select Agent Registry program overseen jointly by USDA and the Centers for Disease Control and Prevention (CDC). Finally, the identification of previously unknown pathogens (such as SARS virus) and variants of known agents (such as pathogens with newly arising antimicrobial resistance patterns [Jones et al., 2008]) has placed increased attention on the effects of emerging disease threats, some of which are zoonotic and raise public-health concerns.

In 2012, the OIE list included 116 animal diseases, of which 25 occur in multiple animal species, 14 in cattle exclusively, 11 in sheep and goats, 11 in

equine, 7 in swine, 12 in birds, and 36 in other species (lagomorphs, bees, fishes, mollusks, crustaceans, and amphibians). The diseases that occur in livestock and poultry are provided in Table 2-1.

In addition to the list of reportable diseases, OIE member countries are expected to notify OIE when a new disease agent is identified or when the epidemiology of a known infectious agent changes significantly. That in effect creates the need for a system that can detect and characterize newly arising disease threats in member countries.

TABLE 2-1 World Organisation for Animal Health List of Animal Diseases, 2012. (Boldface indicates zoonotic diseases; underlining indicates FADs).

Animal	Disease
Multiple Species	Anthrax
	Aujeszký disease
	<u>Bluetongue^a</u>
	Brucellosis (<i>Brucella abortus</i>)
	Brucellosis (<i>Brucella melitensis</i>)
	Brucellosis (<i>Brucella suis</i>)
	<u>Crimean-Congo hemorrhagic fever</u>
	Echinococcosis/hydatidosis
	Eastern equine encephalomyelitis
	Epizootic hemorrhagic disease
	<u>Foot-and-mouth disease</u>
	Heartwater
	<u>Japanese encephalitis</u>
	<u>New World screwworm (<i>Cochliomyia hominivorax</i>)</u>
	<u>Old World screwworm (<i>Chrysomya bezziana</i>)</u>
	Paratuberculosis
	Q fever
	Rabies
	<u>Rift Valley fever</u>
	Rinderpest (eradicated)
	<u>Surra (<i>Trypanosoma evansi</i>)</u>
	Trichinellosis
	Tularemia
	<u>Vesicular stomatitis^a</u>
	West Nile fever
	Cattle
Bovine babesiosis	
Bovine genital campylobacteriosis	
<u>Bovine spongiform encephalopathy</u>	
Bovine tuberculosis	
<u>Contagious bovine pleuropneumonia</u>	
Enzootic bovine leukosis	
<u>Haemorrhagic septicemia</u>	
Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis	
<u>Lumpy skin disease</u>	
<u>Theileriosis</u>	
Trichomonosis	
<u>Trypanosomosis</u> (tsetse-transmitted)	

(Continued)

TABLE 2-1 Continued

Animal	Disease	
Equine	<u>African horse sickness</u>	
	<u>Contagious equine metritis</u>	
	<u>Dourine</u>	
	Equine infectious anemia	
	Equine influenza	
	<u>Equine piroplasmosis</u>	
	Equine rhinopneumonitis	
	Equine viral arteritis	
	<u>Glanders</u>	
	<u>Venezuelan equine encephalomyelitis</u>	
	<u>Western equine encephalomyelitis</u>	
	Sheep or goat	Caprine arthritis/encephalitis
		Contagious agalactia
<u>Contagious caprine pleuropneumonia</u>		
Enzootic abortion of ewes (ovine chlamydiosis)		
Maedi-visna		
<u>Nairobi sheep disease</u>		
Ovine epididymitis (<i>Brucella ovis</i>)		
<u>Peste des petits ruminants</u>		
<u>Salmonellosis (<i>Salmonella abortusovis</i>)</u>		
Scrapie		
<u>Sheep pox and goat pox</u>		
Swine	<u>African swine fever</u>	
	<u>Classical swine fever</u>	
	<u>Nipah virus encephalitis</u>	
	Porcine cysticercosis	
	Porcine reproductive and respiratory syndrome	
	Swine vesicular disease	
Transmissible gastroenteritis		
Avian	Avian chlamydiosis	
	Avian infectious bronchitis	
	Avian infectious laryngotracheitis	
	Avian mycoplasmosis (<i>Mycoplasma gallisepticum</i>)	
	Avian mycoplasmosis (<i>Mycoplasma synoviae</i>)	
	Duck virus hepatitis	
	Fowl typhoid	
	<u>Highly pathogenic avian influenza</u> and low pathogenic avian influenza in poultry per Chapter 10.4. of the <i>Terrestrial Animal Health Code</i>	
	Infectious bursal disease (Gumboro disease)	
	<u>Exotic Newcastle disease</u> ^b	
Pullorum disease		
Turkey rhinotracheitis		

SOURCE: OIE (2012).

NOTES: ^aSome viral serotypes of bluetongue and vesicular stomatitis are endemic in the United States; others are considered exotic.^bExotic Newcastle disease virus is technically zoonotic, as it can infect humans and cause mild clinical illness such as conjunctivitis and oral lesions (Chang, 1981; Alexander, 2000).

In 2004, the White House Office of Science and Technology Policy and the RAND Corporation convened a blue ribbon panel to assess the threat of biological terrorism to livestock and poultry. The results of the panel deliberations on high-priority and medium-priority threats are provided in Table 2-2.

TABLE 2-2 Priority List of Diseases of Concern. (Boldface indicates zoonotic diseases; underlining indicates FADs).

Priority Level	Disease or Agent
High	Foot-and-mouth disease
	Highly pathogenic avian influenza
	Exotic Newcastle disease
	Classical swine fever
	Nipah virus
	Hendra virus
Medium	Rift Valley fever virus
	Rinderpest (eradicated)
	African swine fever
	Venezuelan equine encephalomyelitis
	Transmissible spongiform encephalopathies
	Pox viruses
	Unknown or emerging diseases

SOURCE: Kelly et al. (2004).

Of note in Table 2-2 is the inclusion of Nipah virus, Hendra virus, and Rift Valley fever virus as high-priority pathogens, which are also zoonotic agents, and the inclusion of Venezuelan equine encephalomyelitis viruses, pox viruses, and unknown or emerging diseases as having medium priority.

The United States has also compiled a list of 17 diseases or agents for the national vaccine stockpile that are considered threats in connection with intentional or accidental introduction (Table 2-3). This list reflects agents for which immediate vaccine preparedness and deployment is prioritized, and includes agents not found on the OIE list (such as Hendra and Akabane viruses). All but eastern equine encephalomyelitis and Q fever are considered FADs, and many are zoonotic.

DIAGNOSTIC NEEDS

In 2002, in conjunction with the development and implementation of the National Animal Health Laboratory Network (NAHLN), eight agents were identified for which deployment of rapid and accurate diagnostic tests had high priority: foot-and-mouth disease virus, CSF virus, highly pathogenic avian influenza virus, exotic Newcastle disease virus, African swine fever virus, rinderpest virus, lumpy skin disease virus, and *Mycoplasma mycoides* subsp. *mycoides* SC (bovine biotype), the causative agent of contagious bovine pleuropneumonia. In

TABLE 2-3 Most Serious Animal Disease Threats in the United States Listed on the National Vaccine Stockpile List. (Boldface indicates zoonotic diseases).

Animal	Disease or Agent
Avian	Highly pathogenic avian influenza
Multiple species	Foot-and-mouth disease
Multiple species	Rift Valley fever
Avian	Exotic Newcastle disease
Multiple species	Nipah virus
Multiple species	Hendra virus
Swine	Classical swine fever
Cattle	Bovine spongiform encephalopathy
Multiple species	Rinderpest (eradicated)
Multiple species	Japanese encephalitis
Equine	African horse sickness
Equine	Venezuelan equine encephalomyelitis
Swine	Contagious bovine pleuropneumonia
Multiple species	Heartwater (<i>Ehrlichia ruminantium</i>)
Equine	Eastern equine encephalomyelitis
Multiple species	Q fever (<i>Coxiella burnetii</i>)
Cattle, sheep, and goat	Akabane virus

addition, DHS conducted a series of workshops examining the needs for live-stock and poultry disease screening tools. The results of those workshops (see Box 2-1), the latest of which occurred in May 2012, have helped to identify agents for which diagnostic test development is of highest priority and have directed the development of diagnostic test formats and sample types that will be of the greatest value for disease detection and response.

The workshops provide a current perspective on the high-priority research needs identified by stakeholders for diagnostic test development to counter disease threats. A facility in which to conduct such research will require high-level biocontainment for initial proof of principle and test development.

As indicated in Tables 2-1, 2-2, and 2-3, many agriculturally important diseases are also of human health importance (zoonoses). Recent examples include highly pathogenic avian influenza A(H5N1), which has a 60% case-fatality rate among recognized human infections that have occurred primarily in Asia since 2003. As of May 2, 2012, the World Health Organization received reports of 603 confirmed human cases and 356 deaths due to highly pathogenic avian influenza A(H5N1) (WHO, 2012). Many zoonotic agents, such as eastern and western equine encephalomyelitis viruses, are endemic within the United States, and others, such as West Nile virus, are recent introductions. Some zoonotic pathogens—such as Crimean-Congo hemorrhagic fever, Nipah, and Hendra viruses—require biosafety level 4 containment for their safe and secure handling. Many are recognized as potential bioterrorist agents and are listed as “crossover agents” in the Select Agent Program.

BOX 2-1
Summary of Agricultural Screening Tools
Workshops Sponsored by DHS

The first Agricultural Screening Tools Workshop, held in November 2010 (FAZD, 2010), helped to identify gaps in protecting US agriculture and public health. Priorities for development of screening tools from that workshop were as follows:

- Validate the foot-and-mouth disease and classical swine fever real-time polymerase chain reaction (real-time PCR) assays currently used by the NAHLN for use with additional specimen matrices, specifically:
 - Bovine bulk milk tank samples.
 - Swine and bovine oral fluids.
 - Blood.
- Evaluate and, where possible, validate a procedure for pooling samples with multiple specimen types (matrices).
- Complete validation and deployment of available serological assays for use in proving freedom from disease.
- Support development of a rapid and accurate enzyme-linked immunosorbent assay (ELISA) to differentiate vaccinated from unvaccinated animals that have foot-and-mouth disease.
- Invest in more rapid, detection-sensitive technologies for use in pen-side, premises, and processing-point testing of animals or products. Specifically, continue to evaluate and, if it is warranted, validate commercialized lateral-flow antigen detection devices for foot-and-mouth disease in addition to pursuing the development of alternate portable technologies for pen-side use.
- Invest in newer technologies for screening and continue to evaluate for development and validation.

The second Agricultural Screening Tools Workshop, held in April 2011 (FAZD, 2011), set priorities among the following diagnostic test needs:

- Develop agricultural screening tools that can be used to permit movement of animals that do not have clinical signs of disease, especially during an outbreak or recovery period.
- Validate assays that are currently being used for PCR and ELISA testing for use with additional matrices, including
 - milk (such as from bulk milk tanks).
 - oral fluids (such as from saliva-drenched ropes).
 - meat juice.
 - air and environmental samples.
 - blood (especially for testing for foot-and-mouth disease virus).
- Validate pooling of samples to test for foreign animal diseases, including
 - Optimal pooling of swabs or similar specimens for key high-consequence poultry diseases.
 - Optimal pooling of animal blood or swab samples, especially for foot-and-mouth disease detection.
- Develop simple, low-cost, field-deployable devices for nucleic acid extraction or amplification.
- Develop and validate serological tests for “disease-free” testing and develop associated policies for using those tests.

SOURCES: FAZD (2010, 2011).

AGROTERRORISM

A particular route of entry of FADs that needs to be considered is the deliberate introduction of a native or bioengineered disease agent for the purpose of destabilizing food sources or generating fear. Agroterrorism was the focus of several homeland security presidential directives (HSPD-5 and HSPD-7 in 2003 and HSPD-9 in 2004) and of Congressional Research Service reports (2001, 2004-2007). The Strategic Partnership Program Agroterrorism Initiative was established in 2005 by the Federal Bureau of Investigation (FBI), DHS, USDA, and the Food and Drug Administration (FDA) to include industry partnership. USDA and FDA have Web sites dedicated to the issue (see FDA, 2008; USDA, 2012), and the FBI recently focused attention on agroterrorism in a 2012 *FBI Law Enforcement Bulletin* (Olson, 2012). The latter notes that the terrorist threat analysis now recognizes the increased possibility of smaller, less dramatic, independent attacks, which would include agroterrorism.

If a potential intentional release is reported, health authorities notify USDA's Office of the Inspector General or FDA's Office of Criminal Investigation, which will contact the National Operations Center. If it is determined that the event is terrorism-related, those offices will contact the local FBI weapons of mass destruction unit to launch a full-scale investigation. Aspects of the investigatory process include continued surveillance of the outbreak, maintenance of chain of custody, and identification of appropriate laboratories for sample submission. The Integrated Consortium of Laboratory Networks established by the FBI and CDC comprises the Laboratory Response Network, the Food Emergency Response Network, the NAHLN, and the National Plant Diagnostic Network. As with all response networks, pre-established working relationships facilitate a preliminary cross-check inquiry to identify terrorist attacks in the agriculture sector.

SUMMARY

Numerous National Research Council studies in the last 10 years have assessed disease threats to animal health and public health (NRC, 2005a,b; IOM and NRC, 2009), so the present committee did not attempt an exhaustive reconsideration of the broad array of disease agents that can affect animal agriculture. But the committee emphasizes that the drivers of disease emergence in our global society have not changed, which could give rise to novel agents or to known agents that are exotic to the United States. In general, the committee agrees with conclusions of previous analyses yet emphasizes the need for more cross-cutting, integrated threat assessments that consider multiple variables in a quantitative manner. Foot-and-mouth disease remains a disease of high priority in animal agriculture because of its propensity to spread rapidly and its potentially devastating economic consequences. But foot-and-mouth disease is not the

only threat, and a comprehensive system to counter such threats in animal agriculture is vital. In Chapter 3, the committee describes an ideal system for addressing such threats and identifies critical core capabilities necessary in a national laboratory.

REFERENCES

- Alexander, D.J. 2000. Newcastle disease and other avian paramyxoviruses. *Reviews of Science and Technology* 19:443-462.
- Blake, A., M.T. Sinclair, and G. Sugiyarto. 2003. Quantifying the impact of foot and mouth disease on tourism and the UK economy. *Tourism Economics* 9(4):449-465.
- Blayney, D.P., J. Dyck, and D. Harvey. 2006. Economic Effects of Animal Diseases Linked to Trade Dependency [online]. Available: <http://www.ers.usda.gov/AmberWaves/April06/Features/AnimalDisease.htm> (accessed June 26, 2012).
- BLS (Bureau of Labor Statistics). 2012a. Labor Force Statistics from the Current Population Survey: Employed Persons by Occupation, Sex, and Age [online]. Available: <http://www.bls.gov/web/empsit/cpseea19.pdf> (accessed June 8, 2012).
- BLS. 2012b. Labor Force Statistics from the Current Population Survey: Persons at Work in Agriculture and Nonagricultural Industries by Hours of Work [online]. Available: <http://www.bls.gov/web/empsit/cpseea24.pdf><http://www.bls.gov/web/empsit/cpseea19.pdf> (accessed June 8, 2012).
- Carpenter, T.E., J.M. O'Brien, A.D. Hagerman, and B.A. McCarl. 2011. Epidemic and economic impacts of delayed foot-and-mouth disease: A case study of a simulated outbreak in California. *Journal of Veterinary Diagnostic Investigation* 23:26-33.
- Chang, P.W. 1981. Newcastle Disease. In: *CRC Handbook Series in Zoonoses*. Section B: *Viral Zoonoses Volume II*, G.W. Beran, ed. Boca Raton, FL: CRC Press. Pp. 261-274.
- Delgado, C.L., M.W. Rosegrant, H. Steinfeld, S.K. Ehui, and C. Courbois. 1999. Live-stock to 2020: The Next Food Revolution. Food, Agriculture, and the Environment Discussion Paper 28. Washington, DC: International Food Policy Research Institute [online]. Available http://www.ifpri.org/sites/default/files/publications/pubs_2020_dp_dp28.pdf (accessed June 5, 2012).
- Ekboir, J.M. 1999. Potential Impact of Foot-and-Mouth Disease in California: The Role and Contribution of Animal Health Surveillance and Monitoring Services. Davis, CA: University of California Agricultural Issues Center [online]. Available: <http://aic.ucdavis.edu/pub/fmd.html> (accessed June 6, 2012).
- FAO (Food and Agricultural Organization of the United Nations). 2009. How to Feed the World in 2050, High Level Expert Forum, October 12-13, 2009. Italy, Rome: FAO [online]. Available: http://www.fao.org/fileadmin/templates/wsfs/docs/Issues_papers/HLEF2050_Global_Agriculture.pdf (accessed June 5, 2012).
- FDA (US Food and Drug Administration). 2008. Strategic Partnership Program Agroterrorism (SPPA) Initiative - Final Summary Report September 2005-September 2008. US Food and Drug Administration [online]. Available: <http://www.fda.gov/Food/FoodDefense/FoodDefensePrograms/ucm170509.htm> (accessed June 6, 2012).

- FAZD (National Center for Foreign Animal and Zoonotic Disease Defense). 2010. Protecting Agricultural Infrastructure: Defining the Needs and Requirements for Agricultural Screening Tools [online]. Available: <http://fazd.tamu.edu/files/2011/01/AST-Workshop-Report-FAZD-Center-FINAL-1.2011.pdf> (accessed June 27, 2012).
- FAZD. 2011. Enhancing Ag Resiliency: The Agricultural Industry Perspective of Utilizing Agricultural Screening Tools [online]. Available: <http://fazd.tamu.edu/files/2011/06/ASTII-Report-FINAL.pdf> (accessed June 27, 2012).
- IOM (Institute of Medicine) and NRC (National Research Council). 2009. Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases. G.T. Keusch, M. Pappaioanou, M.C. Gonzalez, K.A. Scott, and P. Tsai, eds. Washington, DC: The National Academies Press.
- Jones, K.E., N.G. Patel, M.A. Levy, A. Storeygard, D. Balk, J.L. Gittleman, and P. Daszak. 2008. Global trends in emerging infectious diseases. *Nature* 451(7181):990-993.
- Kelly, T.K., P. Chalk, J. Bonomo, J. Parachini, B.A. Jackson, and G. Cecchine. 2004. The Office of Science and Technology Policy Blue Ribbon Panel on the Threat of Biological Terrorism Directed against Livestock. CF-193-OSTP. Arlington, VA: RAND Corporation [online]. Available http://www.rand.org/pubs/conf_proceedings/2005/CF193.sum.pdf (accessed May 29, 2012).
- National Research Council (NRC). 2005a. Animal Health at the Crossroads: Preventing, Detecting, and Diagnosing Animal Diseases. Washington, DC: The National Academies Press.
- NRC. 2005b. Critical Needs for Research in Veterinary Science. Washington, DC: The National Academies Press.
- OIE (World Organisation for Animal Health). 2012. OIE Listed Diseases [online]. Available: <http://www.oie.int/animal-health-in-the-world/oie-listed-diseases-2012/> (accessed May 2, 2012).
- Olson, D. 2012. Agroterrorism: Threats to America Economy and Food Supply. FBI Law Enforcement Bulletin, February 2012 [online]. Available: <http://www.fbi.gov/stats-services/publications/law-enforcement-bulletin/february-2012/agroterrorism> (accessed June 6, 2012).
- Paarlberg, P.L., J.G. Lee, and A.H. Seitzinger. 2002. Potential revenue impacts of a foot-and-mouth disease outbreak in the United States. *Journal of American Veterinary Medical Association* 220(7):988-992.
- Thompson, D., P. Muriel, D. Russell, P. Osborne, A. Bromley, M. Rowland, S. Creigh-Tyte, and C. Brown. 2002. Economic costs of the foot and mouth disease outbreak in the United Kingdom in 2001. *Reviews of Science and Technology* 21(3):675-687.
- UK Defra (UK Department of Environment, Food, and Rural Affairs). 2002. Origin of the UK Foot and Mouth Disease Epidemic in 2001. United Kingdom Department of Environment, Food, and Rural Affairs [online]. Available: <http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/fmdorigins1.pdf> (accessed June 5, 2012).
- United Nations. 2011. World Population to Reach 10 Billion by 2100 if Fertility in all Countries Converges to Replacement Level. United Nations Press Release: May 3, 2011 [online]. Available: http://esa.un.org/unpd/wpp/Documentation/pdf/WPP2010_Press_Release.pdf (accessed June 5, 2012).
- USDA (US Department of Agriculture). 2012. Strategic Partnership Program Agroterrorism (SPPA) [online]. Available: http://www.usda.gov/wps/portal/usda/usdahome?contentidonly=true&contentid=content_sppa.html (accessed June 6, 2012).

- USDA-APHIS (US Department of Agriculture, Animal and Plant Health Inspection Service). 2012. Summary of Recent FAD Investigations [online]. Available: http://www.aphis.usda.gov/animal_health/emergency_management/downloads/summary_fad_investigations.pdf (accessed June 27, 2012).
- USDA-ERS (US Department of Agriculture, Economic Research Service). 2011. Food Consumer Price Index and Expenditures: Table 7 - Food Expenditures by Families and Individuals as a Share of Disposable Personal Income [online]. Available: http://www.ers.usda.gov/briefing/cpifoodandexpenditures/data/Expenditures_tables/table7.htm (accessed June 5, 2012).
- USDA-ERS. 2012a. Farm, Rural, and Natural Resources Indicators. Amber Waves [online]. Available: <http://www.ers.usda.gov/AmberWaves/June12/Indicators/Indicators.htm> (accessed June 8, 2012).
- USDA-ERS. 2012b. Livestock, Dairy, and Poultry Outlook: Cattle Prices Decline Following Extended Poor Packer Margins. April 16, 2012 [online]. Available: <http://www.ers.usda.gov/publications/ldp/2012/04Apr/LDPM214.pdf> (accessed June 5, 2012).
- USDA-FAS (US Department of Agriculture, Foreign Agricultural Service). 2011. South Korean Foot and Mouth (FMD) Outbreak Likely to Impact Global Pork and Grain Trade [online]. Available: <http://www.fas.usda.gov/info/IATR/Formatted%20IATR%20South%20Korea%20FMD%202011.pdf> (accessed July 9, 2012).
- WHO (World Health Organization). 2012. Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2012 [online]. Available: http://www.who.int/influenza/human_animal_interface/EN_GIP_20120502CumulativeNumberH5N1cases.pdf (accessed June 8, 2012).
- Zhao, Z., T.I. Wahl, and T.L. Marsh. 2006. Invasive Species management: foot-and-mouth disease in the US Beef industry. *Agricultural and Resource Economics Review* 35(1):98-115.

3

An Integrated National System for Addressing Foreign Animal Diseases and Zoonotic Diseases

US federal agencies have a responsibility for and a vital role in the prevention, detection, and control of foreign animal diseases (FADs) and zoonotic diseases that have the potential for broad health and socioeconomic effects. Historically, the US Department of Agriculture (USDA) has addressed disease threats to the agricultural animal industries that may occur as a result of introduction of an FAD, and confronting the potential human health effects of zoonotic diseases has been the responsibility of the Department of Health and Human Services. Although the historical mandates of those agencies have not changed, the disease threats have. The threat of bioterrorism, heightened after the events of September 11, 2001; the later creation of the Department of Homeland Security (DHS); and advances in biotechnology that have increased the risk of purposeful or inadvertent modifications of microorganisms that could increase virulence, expand host range, or enhance transmissibility (Berns et al., 2012; Enserink and Cohen, 2012) have drawn the world's attention to the threat of disease outbreaks. Our growing global interconnectivity; the growing global population; the demand for food, particularly animal-based protein; and increasing contact with wild ecosystems through land development make it likely that emerging and re-emerging pathogens will continue to occur and spread at an even greater rate. Scientists predict that two to four new pathogens will emerge each year and that RNA viruses, especially those at the human-animal interface, will present the greatest threat (Brownlie et al., 2006). The factors that could create "the perfect microbial storm", as described by the Institute of Medicine (IOM, 2003), are still in place and intensifying, and this suggests that the risk of disease incursion continues to increase and that the implications are even more profound. The impact of those factors has been felt on local to global levels, and has resulted in policy changes in disease reporting by such international agencies as the World Health Organization (WHO) through the codification of the

International Health Regulations in 2005 (WHO, 2007) and the revised list of notifiable diseases (see Table 2-1 in Chapter 2) and requirements for notification of emerging diseases by the World Organisation for Animal Health (OIE, 2010). Commensurate with those changes is an expectation that WHO and OIE member countries will have a reliable infrastructure for disease surveillance and response (Fidler, 2005; Baker and Fidler, 2006).

As noted in Chapter 2, a number of previous National Research Council (NRC) and IOM studies have addressed current threats to our nation's health and welfare, including both FADs and zoonotic diseases (IOM, 2003). A recent IOM and NRC report, *Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases* (2009), is of particular relevance and recommended several actions to strengthen the global capacity for addressing disease threats. The recommendations included improved use of information technology (Recommendation 1-2), a strengthened global laboratory network (Recommendation 1-3), and expanded human-resource capacity (Recommendation 1-4) to support disease surveillance and response (IOM and NRC, 2009). The recommendations for a global system apply equally to the framework for animal-disease surveillance and response within the United States, whether for zoonotic diseases or FADs. Protecting US animal agriculture requires a well-integrated system that spans authorities, geography, and many programs and activities. The idea that a chain is only as strong as its weakest link applies to the complex systems needed to protect animal agriculture from the incursion of serious diseases and to address a riskier world.

THE ROLE OF A NATIONAL LABORATORY FACILITY IN AN INTEGRATED SYSTEM

Critical Core Functions

The committee considered its task in the context of an integrated system in the United States for addressing FAD and zoonotic disease threats and the role of a national biocontainment laboratory in such a system. The ideal system would capture and integrate the substantial human and physical assets distributed throughout the nation to optimally address the threat of FADs and zoonotic diseases. It would include surveillance and detection, diagnostics, and disease response and recovery and would have research and development and training of the workforce as critical core elements to support each of these functional arms (see Figure 3-1). These elements would provide the capabilities needed to support multiple disease-control strategies, the choice of which is dependent on many factors such as the likelihood of introduction to the United States, disease spread rates, and cost and effectiveness of control. A robust laboratory infrastructure underlies all those components. A national role in the coordination of the system is essential, and a federal laboratory or network of laboratories would be the cornerstone of the system. The ideal system would reach beyond our borders to tap the expertise and resources of the global infectious-disease surveil-

AN INTEGRATED NATIONAL SYSTEM FOR ADDRESSING DISEASES 37

lance, diagnostic, and research communities. Recognizing the threat posed by zoonotic diseases and the known and potential roles of animals in maintaining and transmitting infectious agents, the ideal system would capture both human- and animal-health expertise and laboratory infrastructure to achieve the common goals of disease recognition and response.

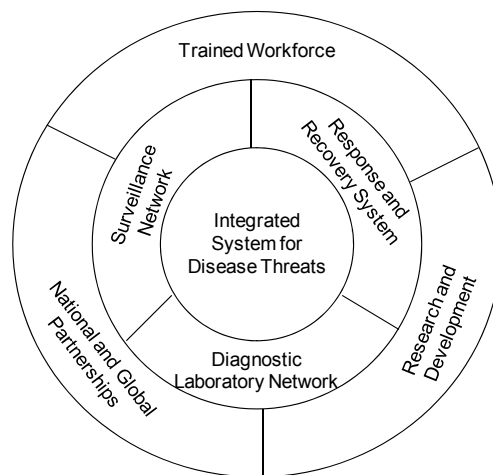


FIGURE 3-1 Components of an integrated national system for addressing foreign animal disease and zoonotic disease threats. Laboratory infrastructure underlies all components.

Surveillance

At the heart of early recognition of a newly introduced disease, whether its occurrence is intentional or natural, is the ability to gather and access data from the field. Technology for capturing the billions of bits of information flowing through electronic channels every day can help to detect unusual events in real time, but it is unlikely that a technology-based approach to data acquisition will ever be the sole or most accurate means by which we can recognize a disease occurrence in the United States. Human resources and a trained workforce are vital to early recognition and verification of an emerging disease event. It is essential to ensure that trained personnel, both professional and lay, are well versed in the manifestations of known diseases in animals and humans and attuned to the variations in disease expression that can indicate a newly emerging disease event. The various clinical signs and pathological changes caused by FAD and zoonotic disease agents can be demonstrated effectively with experimental inoculation of animals, and many FAD and zoonotic disease agents require animal biosafety level 3 (ABSL-3), biosafety level 3 agriculture (BSL-3Ag), or ABSL-4 containment for live-animal work; so training of the workforce in early detection is an essential function that should be provided by a cen-

tral laboratory that has appropriate biocontainment (see Box 3-1 for the description of biosafety levels). The committee agreed that the strategic use of video imaging, plastination (fixation, dehydration, impregnation, and hardening of tissues), and other technological means to capture and broadly disseminate training materials through electronic media, and engagement of the workforce in disease-control campaigns in regions that are endemic for animal diseases or that experience outbreaks of diseases foreign to the United States could reduce the need for hands-on training with experimentally infected animals and thereby reduce the need for training space in the proposed NBAF.

BOX 3-1

Laboratory Biosafety Levels and Types of Pathogens Handled at Each Level as defined in *The Biosafety in Microbiological and Biomedical Laboratories*, 5th Edition

Biosafety Level 1 (BSL-1): Biosafety Level 1 is suitable for work involving well-characterized agents not known to consistently cause disease in immunocompetent adult humans, and present minimal potential hazard to laboratory personnel and the environment.

Biosafety Level 2 (BSL-2): Biosafety Level 2 builds upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. It differs from BSL-1 in that: 1) laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; 2) access to the laboratory is restricted when work is being conducted; and 3) all procedures in which infectious aerosols or splashes may be created are conducted in biosafety cabinets or other physical containment equipment.

Biosafety Level 3 (BSL-3): Biosafety Level 3 is applicable to clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure.

Animal Biosafety Level 3 (ABSL-3): Animal Biosafety Level 3 involves practices suitable for work with laboratory animals infected with indigenous or exotic agents, agents that present a potential for aerosol transmission, and agents causing serious or potentially lethal disease.

Biosafety Level 3 Enhanced (BSL-3E): Situations may arise for which enhancements to BSL-3 practices and equipment are required; for example, when a BSL-3 laboratory performs diagnostic testing on specimens from patients with hemorrhagic fevers thought to be due to dengue or yellow fever viruses. When the origin of these specimens is Africa, the Middle East, or South America, such specimens might contain etiologic agents, such as arenaviruses, filoviruses, or other viruses that are usually manipulated in a BSL-4 laboratory. Examples of enhancements to BSL-3 laboratories might include: 1) enhanced respiratory protection of personnel against aerosols; 2) high-efficiency particulate air filtration of dedicated exhaust air from the laboratory; and 3) personal body shower.

(Continued)

Box 3-1 Continued

Biosafety Level 3 Agriculture (BSL-3Ag): In agriculture, special biocontainment features are required for certain types of research involving high consequence livestock pathogens in animal species or other research where the room provides the primary containment. To support such research, the US Department of Agriculture has developed a special facility designed, constructed and operated at a unique animal containment level called BSL-3Ag. Using the containment features of the standard ABSL-3 facility as a starting point, BSL-3Ag facilities are specifically designed to protect the environment by including almost all of the features ordinarily used for BSL-4 facilities as enhancements.

Biosafety Level 4 (BSL-4)¹: Biosafety Level 4 is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments, or a related agent with unknown risk of transmission. Agents with a close or identical antigenic relationship to agents requiring BSL-4 containment must be handled at this level until sufficient data are obtained either to confirm continued work at this level, or re-designate the level.

SOURCE: CDC (2009).

Training at a national facility can be supplemented, for example, with

- USDA Animal and Plant Health Inspection Service (APHIS) online resources.²
- The online FAD information and Emerging and Exotic Diseases of Animals (EEDA) course provided by the Center for Food Security and Public Health at Iowa State University.³
- The Foreign Animal Disease Training Course at Colorado State University.⁴
- The Foreign Animal, Emerging Diseases course at the University of Tennessee College of Veterinary Medicine.⁵

¹The designation “ABSL-4 large animal” is a terminology used by DHS to specify areas where biosafety level 4 research in large animals is conducted, but this term has not been codified by the BMBL.

²URL: http://www.aphis.usda.gov/emergency_response/NAHEM_training/index_nahem.shtml (accessed June 1, 2012).

³URL: <http://www.cfsph.iastate.edu/EEDA-Course/> (accessed June 1, 2012). The EEDA Web-based course was developed in 2000-2002 by Iowa State University, the University of Georgia, the University of California, Davis, and USDA. It has been used since 2002 in US veterinary schools to raise awareness of foreign, emerging, and exotic animal diseases and the appropriate responses if an unusual disease is suspected. The EEDA book is provided to all students at veterinary colleges and schools in the United States through funding from APHIS.

⁴URL: <http://www.cvmbs.colostate.edu/aphi/> (accessed June 5, 2012).

- Continuing-education courses, such as Response to Emergency Animal Diseases in Wildlife,⁶ and other online and digital media sources of FAD information (such as a CD on FADs provided by the National Center for Animal Health Emergency Management).⁷
- Core or elective courses in FADs that are required to be in the curricula of the 28 accredited colleges and schools of veterinary medicine in North America.
- Specialized courses in FAD recognition, such as the Smith-Kilborne FAD course offered at the Cornell University College of Veterinary Medicine and Plum Island Animal Disease Center (PIADC).⁸

Box 3-2 summarizes current FAD courses offered at PIADC.

BOX 3-2
Training Courses Offered at the Plum Island Animal Disease Center

Foreign Animal Disease Diagnostics Course

The regular Foreign Animal Disease Diagnostics (FADD) course is intended to train veterinarians employed by federal agencies (mostly USDA-APHIS Veterinary Services), by states, and by the military (primarily the Army Veterinary Corps). The FADD training course is provided three times a year with a maximum participation of 30 veterinarians each time. Today, federal, state, and military veterinarians take the same course (the military Transboundary Animal Diseases (TAD) course was separate for several years). The course includes live experimental animal demonstrations of 11 important livestock diseases (such as foot-and-mouth disease, classical swine fever, exotic Newcastle disease, and highly pathogenic avian influenza) and lectures on 23 diseases of livestock and poultry species. It also covers lectures and demonstrations on the use of personal protective equipment; on-farm disease investigation; collection, packaging, and mailing of diagnostic samples; and administrative procedures related to disease investigation, reporting, and emergency response.

Veterinary Laboratory Diagnostician Course

A separate 1-week course is offered to faculty and residents of US veterinary colleges and schools each year. It follows the same format as the FADD course. Participants do not spend much time in USDA-APHIS administrative training, and they do not become FAD diagnosticians.

(Continued)

⁵URL: <http://www.veterinarypracticenews.com/vet-breaking-news/foreign-animal-emerging-disease-course.aspx> (accessed June 6, 2012).

⁶URL: http://www.aphis.usda.gov/animal_health/prof_development/ (accessed June 4, 2012).

⁷Jon Zack, USDA-APHIS, pers. comm., June 1, 2012.

⁸URL: http://www.aphis.usda.gov/animal_health/prof_development/smith_kilborne.shtml (accessed May 31, 2012).

BOX 3-2 Continued**International Transboundary Animal Diseases Course**

The International Transboundary Animal Disease (ITAD) course is organized and funded through USDA-APHIS International Services (in contrast with the above courses, which are organized and funded through USDA-APHIS Veterinary Services). The course has been given 11 times, once almost every year, with up to 30 international veterinarians each time. It has been delivered completely in Spanish six times. Participants are selected by veterinary and agricultural attachés from among government or academic veterinarians around the world. As in the case of the FADD and the Veterinary Laboratory Diagnostician courses, there is no fee to attend this course; the participants' sponsoring institutions pay for associated travel, lodging, and meals. The ITAD course follows the same schedule and animal demonstrations as the regular FADD course, except that participants do not spend time on USDA-APHIS administrative policies and procedures; instead, they are exposed to discussion on international trade, epidemiology, and emergency response.

Smith-Kilborne Foreign Animal Disease Course

This course in the current format has been delivered for 10 years and includes one veterinary student (after completion of their second year) from each of the 28 US colleges and two international veterinary students (from Canada or Mexico). The Smith-Kilborne program is designed to acquaint veterinary students with various FADs that potentially threaten our domestic animal population. The course includes classroom presentations for 3 days at Cornell University College of Veterinary Medicine on diseases and their implications and 2 days of laboratory experience at the PIADC, where participants observe foot-and-mouth disease, African horse sickness, highly pathogenic avian influenza, and exotic Newcastle disease. The PIADC portion of the course coincides with the first week of a regular FADD course, and experimentally infected animals are shared by the two courses. Students practice necropsies on poultry only. After the course, students are expected to share their new knowledge by giving seminars at their colleges.

Apart from the need to maintain a trained and ready workforce and a potential research and development requirement to support this component, field-based surveillance itself does not require high-biocontainment (BSL-3 and BSL-4) space, although case or outbreak investigations of zoonoses may require use of appropriate personal protective equipment (PPE).

Diagnostics

Historically, the National Veterinary Services Laboratories (NVSL) at Ames, Iowa have provided support for diagnosis of endemic “program diseases”⁹ in the United States by qualified and approved nonfederal laboratories. Training programs for laboratory personnel, proficiency testing, and reference

⁹Program diseases are those designated as “necessary to bring under control or eradicate from the United States” (APHIS, 2012).

reagents have been valuable contributions to state laboratories' ability to perform diagnostic testing for control programs targeting such endemic diseases as brucellosis, pseudorabies, tuberculosis, and equine infectious anemia. The role of the NVSL Foreign Animal Disease Diagnostic Laboratory (FADDL), which is co-located with USDA-ARS and DHS at the PIADC, has been more limited in that it has focused on FADs, for which nonfederal laboratories were not allowed to perform diagnostic testing. The development of the National Animal Health Laboratory Network (NAHLN) in 2002 and associated changes in policy (Memorandum 580.4)¹⁰ now allow state laboratories to conduct diagnostic testing for FADs. Box 3-3 provides an overview of the NAHLN from its inception to the present.

The NAHLN is an excellent example of an integrated system that was created to address the nation's needs, in this case for diagnostic support for early detection, response to an outbreak, and recovery. With the implementation of the NAHLN, the NVSL laboratories at the National Centers for Animal Health (NCAH) in Ames, Iowa, and FADDL at Plum Island now play a vital and irreplaceable role in supporting testing for FADs in approved NAHLN laboratories. Initial test validation (including analytical assessment with samples collected from experimentally infected animals, diagnostic sensitivity, and specificity determination with samples obtained from outbreaks in endemic areas outside the United States, which can be handled only at PIADC and NCAH), reference-reagent production, and proficiency testing are all examples of the critical core functions best managed by a federal laboratory in support of diagnostic testing on a nationwide basis in qualified laboratories. Continued assessment of validated assays against newly arising variants obtained from outbreaks outside the United States also requires adequate biocontainment. For foot-and-mouth disease, this is performed in a federal facility approved for handling of foot-and-mouth disease virus (FMDv).

Finally, the role of NVSL in confirmatory diagnosis of the index case of an FAD cannot be overvalued. Because of the inevitable effects on lives and livelihoods, the index case of a new disease in the United States must be officially reported by a federal agency. The current role of state NAHLN laboratories in the diagnosis of an index case of a potential FAD is to obtain a test result that is actionable but presumptive; appropriate samples are also sent to NVSL, Ames or Plum Island for confirmation. Assays such as cell culture used for confirmatory diagnosis result in amplification of a virus that may be highly contagious and requires a modern, high-biocontainment laboratory environment like that proposed for the NBAF. The ability to culture live FAD pathogens like FMDv for characterization and reference is a critical core function of a national biocontainment laboratory.

¹⁰URL: http://www.aphis.usda.gov/animal_health/lab_info_services/downloads/VSMemo580_4.pdf (accessed May 31, 2012).

BOX 3-3**The National Animal Health Laboratory Network**

The National Animal Health Laboratory Network (NAHLN), launched in 2002, is a cooperative effort of the US Department of Agriculture (USDA) Animal and Plant Health Inspection Service, the USDA National Institute of Food and Agriculture, and the American Association of Veterinary Laboratory Diagnosticians (AAVLD). The mission of the NAHLN is to provide accessible, timely, accurate, and consistent animal disease diagnostic services nationwide that meet the epidemiological and disease reporting needs of the country. The NAHLN also maintains the capacity and capability to provide laboratory services in the event of an FAD or emerging disease event in the country. The NAHLN focuses on diseases of livestock, but it also responds to disease events in nonlivestock species. The NAHLN has contributed to several surveillance activities and control strategies of national interest. The NAHLN laboratories are the first line of early detection of transboundary diseases and serious zoonotic diseases introduced into the United States.

The origins of the NAHLN are in the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 and Homeland Security Presidential Directive 9 (HSPD-9), both of which called on USDA to establish surveillance systems for animal diseases that would mitigate threats to the nation's agricultural sector.

The USDA Safeguarding Review (NASDARF, 2001) identified the need for a network that would coordinate laboratory capacity at the federal level with the extensive infrastructure of the state and university animal disease diagnostic laboratories. Cooperative agreements were awarded by USDA in May 2002 to 12 state and university diagnostic laboratories for a 2-year period. The NAHLN has grown to 58 laboratories (53 state and five federal) in 40 states (see Figure 3-2), and the capability and capacity of the nation's animal-disease surveillance program have grown with it.

At the federal level, USDA's National Veterinary Services Laboratory (NVSL) laboratory units in Ames, Iowa, and Plum Island, New York (Foreign Animal Disease Diagnostic Laboratory [FADDL]), serve as the national reference and confirmatory laboratory for veterinary diagnostics, and it coordinates the training, proficiency testing, assistance, and prototypes for diagnostic tests that are used in the state NAHLN laboratories. One component of NVSL's contribution to the NAHLN is a "train the trainer" program that has increased the number of personnel in NAHLN laboratories who can perform tests for the diagnosis of FADs. The program, offered at FADDL and NVSL, Ames is an example of the successful collaboration between the NVSL and NAHLN laboratories that has resulted in a national network of laboratory personnel who are trained to perform tests for FADs—a resource that did not exist before the NAHLN.

The state and university animal-disease diagnostic laboratories in the NAHLN perform routine diagnostic tests for endemic animal diseases, and they have received specific approval to perform tests for FADs as a part of the national surveillance strategy. A current example of the NAHLN's value is the diagnosis of the fourth US case of bovine spongiform encephalopathy (BSE), reported by USDA on April 24, 2012. A sample collected from a dairy cow was submitted to the California Animal Health and Food Safety (CAHFS) laboratory at the University of California at Davis,

(Continued)

BOX 3-3 Continued

an NAHLN laboratory that performs BSE testing through a contractual agreement with USDA. When the CAHFS laboratory determined that the sample was positive, suspect, or inconclusive for BSE, it was sent to the NVSL for confirmation. That procedure is routine and conforms with the established protocol outlined in a Veterinary Services memorandum (VS Memorandum 580.4). Thousands of BSE tests have been performed in NAHLN laboratories in support of USDA's BSE surveillance strategy. Similar testing agreements for a wide array of animal diseases—including foot-and-mouth disease, classical swine fever, avian influenza, exotic Newcastle disease, chronic wasting disease and scrapie, swine influenza, pseudorabies, and vesicular stomatitis—have been established with NAHLN laboratories nationwide.

The NAHLN effectively demonstrates the value of collaboration between the federal government and state and university animal-disease diagnostic laboratories and may serve as a template for a new relationship among the Department of Homeland Security, USDA, and the NAHLN. Such a new collaboration could accomplish some of the tasks of the proposed National Bio- and Agro-Defense Facility (NBAF) by using infrastructure that already exists in the state and university veterinary diagnostic network, including facilities, professional expertise, and support.

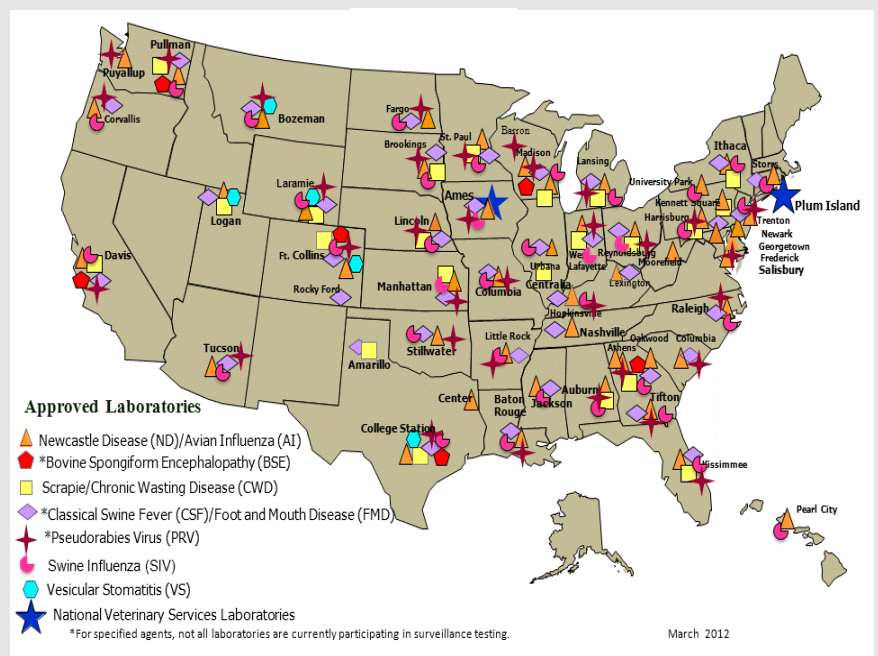


FIGURE 3-2 National Animal Health Laboratory Network. SOURCE: USDA-APHIS (2012).

SOURCE: USDA-APHIS (2012).

Outbreak Response

If the United States identifies a known FAD or a newly emergent disease within its borders, a rapid, comprehensive response is necessary. The type of response will depend on the disease and on whether it is known or newly identified. The historical approach for control of an FAD outbreak has been to quarantine infected premises with diagnostic screening in surrounding zones followed by additional quarantine and diagnostic screening focused on new infected premises with slaughter of infected animals. That approach requires that new cases be rapidly identified with diagnostic assays that have a high level of diagnostic sensitivity and the capability of being performed in a high-throughput manner, particularly in the case of rapidly spreading diseases, such as foot-and-mouth disease. Technological advances in the last few decades have led to the development of direct pathogen identification assays that have very high sensitivity, that target and amplify nucleic acids, and that have the capability of high throughput. The NAHLN has successfully deployed well-validated real-time polymerase chain reaction (PCR) assays for detection of foot-and-mouth disease, avian influenza, pandemic H1N1 influenza, classical swine fever, African swine fever, and rinderpest. That would not have been possible without the support of a federal laboratory: initial validation of the assays was conducted at PIADC, where samples from experimentally inoculated animals were vital for early analytical sensitivity testing. Continuing support for reference reagents, proficiency testing, and ensuring that reagents are available in required quantities to respond to a disease outbreak is fundamental to being prepared and responsive during a real event. It is a function that can best be performed by a federally supported program that includes appropriate laboratory biocontainment.

The United States is increasingly incorporating vaccination into outbreak-response plans for FADs. This scientifically sound and justifiable approach is expected by a populace that increasingly respects the value and welfare of agricultural animals beyond their place in the food chain. Vaccines would probably be used strategically in “ring vaccination” to minimize the number of animals that would need to be killed to control an outbreak. Vaccine development has been going on at PIADC for many years, but as a result of the change in outbreak response and the acceptance of regionalization and compartmentalization by OIE, a higher priority has been attached to vaccine development where gaps exist, and the goal is to develop vaccines that allow differentiation of infected from vaccinated animals (“DIVA” vaccines) and diagnostics. Research on vaccine development for FAD agents requires the ability to grow and manipulate an agent, which in turn requires biocontainment at BSL-3, BSL-3Ag, BSL-3E levels, and—for agents such as Hendra and Nipah viruses, hemorrhagic fever viruses, and some arboviruses—BSL-4 level. Equivalent ABSL containment is required for live-animal work. It is important to note that all the viral agents that require BSL-4 containment are zoonotic; that is, none of the livestock-specific FADs require BSL-4 laboratory containment. Nevertheless, a disease outbreak of a zoonotic virus that requires BSL-4 containment would require appropriate

biocontainment of sufficient capacity to handle the large volume of samples that would be obtained from high-risk animals in the outbreak area, whether in a USDA facility, another government facility, or elsewhere in the United States.

Research and Development

Several examples have been provided above and elsewhere in this report of the need for research and development to support all components of the disease-threat triad. There will be a continuing need for a laboratory that has the capability and the authorization to work with FAD and zoonotic disease agents that require biocontainment at BSL-3Ag, BSL-3E, or BSL-4 levels. Vaccine development for FADs may progress as a disease-control strategy and thus it is also a research endeavor that will require support. The United States will need to consider how vaccines might be used for diseases other than foot-and-mouth disease (for example, African swine fever) and whether additional research is warranted. Not all disease threats will require a vaccine-based approach, but for the ones that do, vaccine research will undoubtedly require animal biocontainment facilities at least for proof-of-concept studies. Continued assessment of diagnostic assays for FADs and zoonotic diseases also requires appropriate facilities, and newly arising variants of these diseases could require animal experiments for addressing transmission levels and shedding, both of which can affect analytic sensitivity and specificity of diagnostic assays.

A newly identified agent will require the utmost caution in biocontainment if it belongs to a viral family of known high virulence and transmissibility (such as Hendra virus when it first appeared as an agent of a new disease of horses and humans in Australia) or, if unknown, appears to have high virulence and transmissibility or that does not have known prophylaxis or treatment. Addressing a newly emergent pathogen will undoubtedly require appropriate biocontainment research facilities, and caution might require a high level of biocontainment, up to BSL-4, for diagnostic development work. When a newly arising FAD or zoonotic disease infectious agent is identified, classical research on pathogenesis, virulence, shedding, transmission, and host range and susceptibility is warranted. Research will probably focus on initial diagnostics and agent characterization during an outbreak to allow time for planning additional experiments aimed at understanding the new agent. After disease control, there will be a need for experiments at a defined, and possibly quite high, biocontainment level, including live-animal experiments even if they are limited to production of reference material for diagnostic assays. A centralized federal facility capable of handling emergent agents will sometimes be required until more is known about modes of transmission among animals and from animals to humans. That need will probably depend on initial characterization of the particular agent involved. Caution is warranted, but so is sound assessment of risk-based scientific evidence.

The recent identification of Schmallerberg virus is a good example of an emergent viral agent that may have predictable transmission patterns characteristic of animal diseases in the virus family Bunyaviridae (Kahn and Line, 2011). The virus has not been identified in the United States, so current policy would prohibit working on it outside a federal facility. If it had occurred in the United States, it might be decided on the basis of scientific evidence that the virus can be investigated safely at a biocontainment level found in many diagnostic, research, and development laboratories in the United States. But if a newly arising flavivirus or hemorrhagic fever virus were identified in the United States, utmost caution would be warranted. The recent incidental finding of Ebola Reston virus in a pig sample from the Philippines that was shipped to PIADC for assistance in diagnosing a disease outbreak demonstrates that a high level of biocontainment for newly emergent pathogens is necessary for safe handling and additional studies.

A key question is the extent to which research with FAD and zoonotic disease agents must be limited to a central national laboratory. It is a policy issue that should be addressed on an agent-specific basis and that will affect capacity needs of a centralized federal facility as part of an integrated system for addressing disease threats. It is clear that research on those diseases can occur both in federal facilities and in other laboratories. In the case of diagnostic assays, collaborative approaches have been successful and have used research protocols that require varied levels of biocontainment for different steps of the validation process. The recent development of an assay to detect FMDv in milk (see Box 3-4) is a salient example of the success of collaboration in using the intellectual capital and infrastructure of university, state, and federal laboratories to address a critical gap related to an FAD agent that requires BSL-3E containment. The opportunity for similar collaboration with higher biocontainment depends on the availability of suitable facilities.

Use of the Broad Research Infrastructure and Intellectual Capital of the World

Coincidentally with changes in the national strategy to detect and respond to the potential incursion of FADs (such as creation of NAHLN and DHS), the United States has realized a marked expansion in biocontainment-laboratory capacity and capability. A substantial number of BSL-3 or higher biocontainment laboratories have been constructed by federal and state agencies, universities, and private companies since 2001. They provide an opportunity for collaborations that maximize national efforts to detect and respond to any incursion of an FAD or zoonotic disease. Furthermore, strategic collaborations with other biocontainment facilities would potentially enhance the efficient use of the proposed NBAF.

BOX 3-4**Detecting Foot-and-Mouth Disease Virus in Milk: A Case Study of Collaboration**

As a result of the second Department of Homeland Security-sponsored Ag Screening Tools Workshop held in April 2011 in Washington, DC (CNA, 2011), stakeholders identified a high-priority need for an assay that would facilitate continuity of business in the dairy and milk processing and distribution industries during a foot-and-mouth disease outbreak. Safe movement of dairy products from production units in or next to the site of infected premises would allow continuity of business and dramatically reduce the overall economic effect of a foot-and-mouth disease outbreak involving the dairy industry. But the safety of milk cannot be ensured without a diagnostic assay that can establish, with high sensitivity, that the milk is free of foot-and-mouth disease virus (FMDv) and that can be performed in high-throughput mode. Such an assay does not exist. It would require that high-throughput extraction procedures be optimized for a milk and cream matrix, that an internal control be used to indicate inhibition of the assay from factors in milk, and that analytical sensitivity, intra-assay variability, and repeatability be assessed.

Recognizing that priority, the National Animal Health Laboratory Network (NAHLN) undertook a diagnostic-test validation project (technically a methods-comparison project) to evaluate and optimize the methods that could be used for high-throughput extraction of RNA from milk and cream and to assess how well the previously validated real-time PCR assay of FMDv approved by NAHLN for use with oral specimens would work with RNA extracted from milk. The proposed project justification and design were reviewed and approved by the NAHLN Methods Technical Working Group. Initial steps in the validation of high-throughput extraction procedures for the assay used a surrogate construct and could be conducted at BSL-2. That allowed early development work to be performed at a state-based NAHLN laboratory (the Wisconsin Veterinary Diagnostic Laboratory). Later steps required the use of live FMDv in milk, and multiple strains of virus were needed for complete assessment. That part of the project required use of a BSL-3Ag facility and was conducted at the Plum Island Animal Disease Center; it highlighted the need for this critical core function to be available at a national laboratory.

The project has moved smoothly through the process of validation with seamless collaboration among federal, university, and state partners. It is nearing completion, and if the results of validation indicate that the assay has the required accuracy, it will be an extremely valuable addition to the diagnostic armamentarium for FMDv. The development of the assay from identification and priority-setting through conception and experimental design to generation of the required data took only about a year. In 2012, interlaboratory assessment and negative cohort studies will determine the robustness and diagnostic specificity of the assay and a negative cohort study to examine diagnostic specificity will be conducted in the field. Both those studies can be conducted in the United States. Final validation will require assessment of diagnostic sensitivity in an endemic area. Review of the data and recommendation to the US Department of Agriculture as to whether the assay is fit for the purpose, what additional studies are needed, and what associated protocols and algorithms for use must be developed before deployment will occur through the Methods Technical Working Group dossier-review process.

(Continued)

BOX 3-4 Continued

The development of the assay is an excellent example of research on new diagnostic assays through collaboration among university, state, and federal laboratories. Nothing was compromised through the collaboration, and the timeline was not prolonged. In fact, it could be argued that the timeline was shortened because of the availability of space and personnel time at the Wisconsin laboratory that might not have been available at the federal laboratory. Assay development required approval of a person from the Wisconsin laboratory to work at PIADC and required 2-3 weeks for technology transfer to PIADC. No additional select-agent personnel approval was required. The entire process can serve as a model for development of assays for which only minimal federal facility biocontainment space is needed. However, it could not be undertaken without appropriate biocontainment for some steps of the methods comparison. In the present example, the biocontainment space had to be at an FMDv-approved facility, and this remains a critical core function in an integrated national system.

Access to modern and functional BSL-3Ag and ABSL-4 large-animal containment facilities is critical to the national strategy to detect and respond to FADs and zoonotic diseases. Figure 3-3 shows the location of some BSL-3, BSL-3Ag, and BSL-4 laboratories in the United States; Table 3-1 lists those and other laboratories that have high-biocontainment space, and where it is known, large-animal capacity space in high biocontainment. The United States has no facility with ABSL-4 large-animal space, and BSL-3Ag (livestock) capability is available at only a few facilities (listed in Table 3-1). All the BSL-4 laboratories that are operational in the United States are also listed in Table 3-1. A number of international laboratories (see Table 3-2) are engaged in research on FADs and zoonotic diseases, and some of them also have ABSL-4 large-animal capability.

To address the disease threat to humans, including zoonoses, the National Institutes of Health (NIH) has assisted in the construction of a network of 13 regional BSL-3 containment laboratories (see Figure 3-3 and Table 3-1). They are generally large facilities that include laboratory space for *in vitro* and *in vivo* research and product-development activities addressing emerging infectious diseases and pathogens of bioterrorism concern. Although their focus is on pathogens of human health importance, some may also affect agriculturally important animals.

An indeterminate number of BSL-3 laboratories exist among the laboratories of the NAHLN and in many academic centers, private research organizations, and commercial firms, but they are generally small and have little or no capacity to handle animals. All the human-oriented biocontainment laboratories have biocontainment space dedicated to *in vitro* research and development, and most have some capability to handle traditional laboratory animals up to small numbers of nonhuman primates.

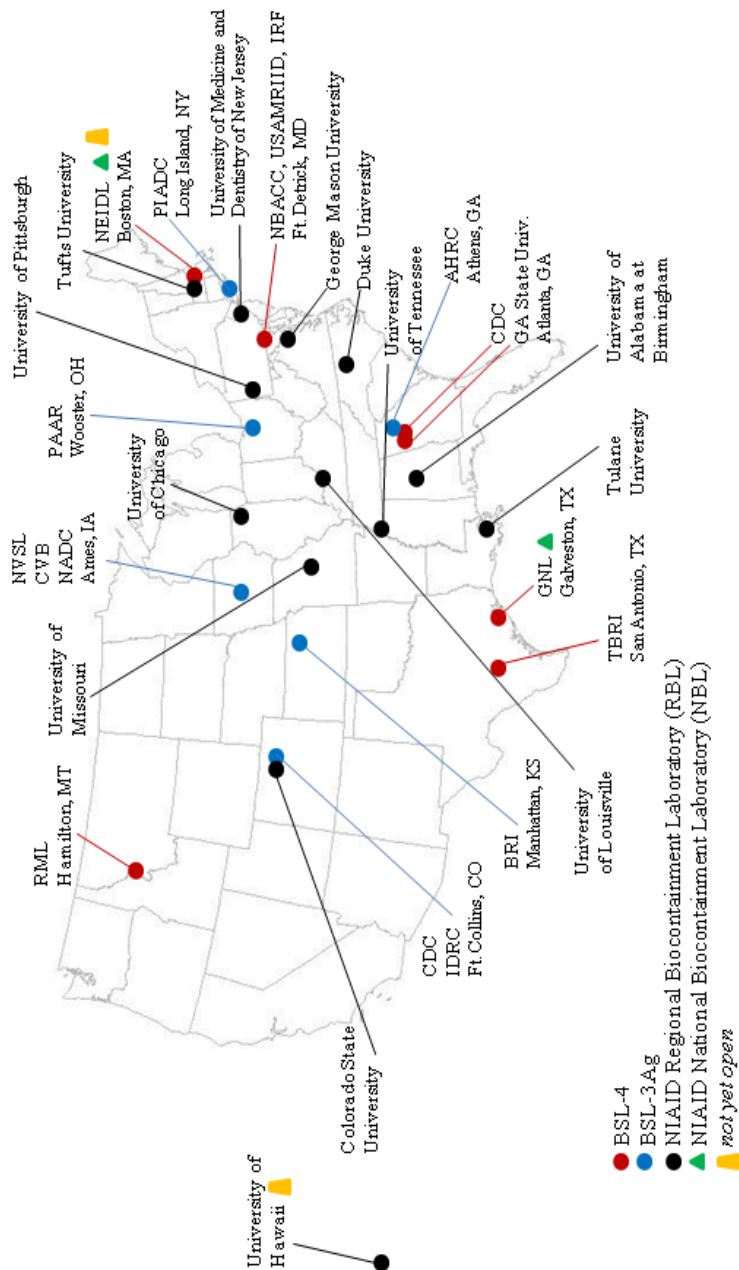


FIGURE 3-3 Selected federal, state, and national biocontainment laboratory (NBL) and regional biocontainment laboratory (RBL) BSL-3, BSL-3Ag, and BSL-4 facilities. Courtesy of Alisha Prather, Galveston National Laboratory, University of Texas Medical Branch.

TABLE 3-1 Selected Federal, State, and University BSL-3Ag, BSL-4, and ABSL-4 Laboratories in the United States and Their Capacity and Capability

Facility Name, Location, and URL	Capacity ^a or Capability	
	BSL-3Ag	BSL-4 or ABSL-4
US Department of Agriculture (USDA) and Other Federal Laboratories		
National Veterinary Services Laboratories (NVSL), Ames, Iowa http://www.aphis.usda.gov/animal_health/lab_info_services/	8,581 ft ² (includes 3,109 ft ² for necropsy suite); total area for NVSL and CVB	None
Centers for Veterinary Biologies (CVB), Ames, Iowa http://www.aphis.usda.gov/animal_health/vet_biologies/	See information above	None
National Animal Disease Center (NADC), Ames, Iowa http://www.ars.usda.gov/Main/docs.htm?docid=3582	17,024 ft ² (includes 2,432 ft ² for necropsy suite)	None
Plum Island Animal Disease Center (PIADC), Long Island, New York http://www.ars.usda.gov/main/site_main.htm?modecode=19-40-00-00	72,400 ft ² (combined BSL-3Ag and BSL-3E)	None
National Biodefense Analysis and Countermeasures Center (NBACC), Ft. Detrick, Maryland; building owned by DHS, but laboratory is managed by a contractor http://www.bnbi.org/	None	BSL-4 (consisting of 24 individual laboratory spaces); total 5,254 ft ² . Four animal rooms (265 ft ² each); total 1,060 ft ² . Four ante rooms (140 ft ² each) total 560 ft ² . Two necropsy suites (225 ft ² each); total 550 ft ² . Capacity: about 2,880 mice, 560 guinea pigs, 42 rabbits per room.
US Army Medical Research Institute for Infectious Diseases (USAMRIID), Ft. Detrick, Maryland http://www.usamrid.army.mil/	None	ABSL-4 for handling traditional laboratory animals, such as small rodents and nonhuman primates. BSL-4 (17,429 ft ²)
USAMRIID (new building under construction)	None	None
Integrated Research Facility (IRF), National Interagency Biodefense Campus of USAMRIID, Ft. Detrick, Maryland http://orf.od.nih.gov/Construction/CurrentProjects/IRF/Detrick.htm	None	One biocontainment block that can be configured at BSL-3 or BSL-4 or combination (11,000 ft ²); eight animal holding rooms with adjacent procedure rooms; intent is to house up to 25 nonhuman primates per room; laboratory not

TABLE 3-1 Continued

<p>National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases (NIAID) Rocky Mountain Laboratory (RML); Hamilton, Montana http://www.niaid.nih.gov/about/organization/dir/rml/pages/overview.aspx</p> <p>Centers for Disease Control and Prevention (CDC), Atlanta, Georgia http://www.cdc.gov/</p>	<p>None</p>	<p>Four BSL-3E/Ag; each BSL-3E/Ag composed of animal holding room (230 ft²), necropsy room (156 ft²), and BSL-3 main laboratory (710 ft²). Cannot work with swine but in an emergency could handle 10-15 lambs in each animal holding room.</p>	<p>BSL-4 can accommodate mice, hamsters, guinea pigs, ferrets, nonhuman primates.</p>	<p>configured for large animals, such as domestic livestock. Not yet fully operational; expected to be declared “substantially complete” by August 2012.</p>
<p>Southeast Poultry Research Laboratory (SEPR), USDA Agricultural Research Service (ARS), Athens, Georgia http://www.ars.usda.gov/main/site_main.htm?modecode=66-12-07-00</p>	<p>None</p>	<p>BSL-3E space: 9,000 ft²; including 10 bench laboratory rooms, seven animal rooms; over 90% of studies are in chickens, turkeys; ducks; remainder in minor poultry species (quail, geese, pheasants), wild birds, a few laboratory mammals; no space for large animals; most studies done in isolation cabinets designed for poultry, other birds.</p>	<p>None</p>	<p>BSL-4: 14,000 ft² of CDC- and USDA-registered and -approved animal research facilities.</p>
<p>NIAID National Biocontainment Laboratories Galveston National Laboratory (GNL), University of Texas Medical Branch; Galveston, Texas http://www.utmb.edu/gnl/</p> <p>National Emerging Infectious Diseases Laboratory (NEIDL); Boston, Massachusetts http://www.bu.edu/neidl/research/</p>	<p>None</p>	<p>None</p>	<p>BSL-4 can accommodate 80 nonhuman primates, 5,000 rodents; not currently operational.</p>	<p>BSL-4: 14,000 ft² of CDC- and USDA-registered and -approved animal research facilities.</p>

(Continued)

TABLE 3-1 Continued

Facility Name, Location, and URL	Capacity ^a or Capability	
	BSL-3Ag	BSL-4 or ABSL-4
Private Laboratory		
Texas Biomedical Research Institute (formerly Southwest Foundation for Biomedical Research), San Antonio, Texas http://tbiomed.org/	One operational ABSL-3 laboratory (2,300 ft ²) can accommodate 60 macaques, 24 marmosets, 12 guinea pigs, 120 rabbits, 3,600 mice.	One operational full-suit ABSL-4 laboratory (1,200 ft ²) can accommodate: 12 macaques, 12 marmosets, 36 guinea pigs, 24 rabbits, 360 mice.
State and University Laboratories		
Animal Health Research Center (AHRC), University of Georgia College of Veterinary Medicine, Athens, Georgia http://www.vet.uga.edu/AHRC/AHRC%20facility%20description.pdf	Eight BSL-3Ag rooms (total 2,840 ft ²), six ABSL-3 animal rooms (total 1,500 ft ²); total all animal rooms 4,340 ft ² ; all laboratories operational and approved for select-agent work.	None
Biosecurity Research Institute (BRI), Kansas State University, Manhattan, Kansas http://www.bri.k-state.edu/	Five BSL-3Ag rooms (10,500 ft ²). Large-animal holding capacity horses, 6-16 (individual housing [I]), 6-22 (group housing [G]); cattle, 18-36 (I), 16-32 (G); sheep, goats, 32 (I), 128-224 (G); pigs, 10-20 (I), 40-100 (G); ferrets, poultry can also be accommodated.	None
Plant Animal Agrosecurity Research (PAAR), Ohio State University, Wooster, Ohio http://oardc.osu.edu/paar/t02_pageview/Home.htm	Four research rooms (each 423 ft ²); associated support spaces include necropsy space (850 ft ²); research spaces built to BSL-3Ag standards; two laboratory spaces (each 242 ft ²) include shower out facility, autoclave access; laboratories built to BSL-3E standards; BSL-3Ag spaces designed to be flexible to incorporate work with agricultural species housed on floor, in cages, isolators or to handle plants as needed.	None

SOURCES: USDA, 2012; Personal communications: J.P. Fitch, NBACC, 05/07/2012; N. Woolfen, USAMRIID, 05/3/2012 and 05/22/2012; P. Jahrling, NIH/NIHID, 05/30/2012; K. Zoon, RML, 05/4/2012; P. Rollin, CDC, 05/8/2012; D. Swayne, USDA-ARS, 05/23/2012; A. Griffiths, Texas Biomedical Research Institute, 05/30/2012; S. Allen, UGA, 05/22/2012; H. Dickerson, UGA, 05/31/2012; and J. Hanson, OARDC-PAAR, 05/7/2012.

^aRoom sizes are net square feet unless indicated otherwise.

TABLE 3-2 Selected International BSL-3Ag and BSL-4Ag/ABSL-4 Laboratories and Their Capacity and Capability^a

Name of Facility	Location/URL	Capacity ^b
Canada		
National Centre for Foreign Animal Disease (NCFAD), Canadian Food Inspection Service	Winnipeg, Canada http://www.nml-1nm.gc.ca/overview-apercu-eng.htm http://www.inspection.gc.ca/english/sci/bio/animal/diag/diag.shtml	BSL-4Ag can take two adult cattle (in the 500-lb range and probably slightly bigger); there are plans to convert one BSL-3Ag cubicle into a BSL-3/4Ag swing space, which would increase BSL-4Ag capacity to six cattle (in two rooms of two and four cattle each).
Australia		
Australian Animal Health Laboratory (AAHL), Commonwealth Scientific and Industrial Research Organisation	East Geelong, Victoria, Australia http://www.csiro.au/en/Organisation-Structure/National-Facilities/Australian-Animal-Health-Laboratory.aspx	BSL-3Ag (9,418 ft ²) Two BSL-4 rooms (1,722.2 ft ² , 505.9 ft ²)
Europe		
Friedrich-Loeffler-Institut (FLI)	Insel Riems, Germany http://www.fli.bund.de/en/startseite/friedrich-loeffler-institut.html	BSL-3Ag facility has eight animal rooms for cattle that can hold a total of 40 cattle with total area of 3,896.5ft ² ; two animal rooms for pigs or small ruminants each can hold 20 pigs or 16 small ruminants with total area of 699.6 ft ² . BSL-4 facility has two animal rooms for cattle that can hold eight cattle (or other livestock species), with total area of 1,420.8 ft ² .
Institute for Animal Health (IAH)	Pirbright, UK http://www.iah.ac.uk/	High-containment animal facilities comply with what United States calls BSL-3Ag+. Animal holding rooms for ruminants, pigs, cattle. Total SAPO 4 area approximately 9,536.8 ft ² . Future facilities at Pirbright high-containment laboratory for small animals, including future work on highly pathogenic avian influenza.

(Continued)

TABLE 3-2 Continued

Name of Facility	Location/URL	Capacity ^b
Institute of Virology and Immunophylaxis (IVI)	Switzerland http://www.bvet.admin.ch/fivi/?lang=en	Total capacity at 100% occupancy is up to 70 cattle and up to 112 sheep, pigs, or goats at ABSL-3 (would not run facility at 100%—more likely at 60%—because of need to have space for emergency situations). All animal isolation facilities are fully operational. BSL-3Ag facility has four pig stables and four cattle stables; maximum number cattle per stable, four; maximum number pigs depends on size of animals. Stable surface: about 430.6 ft ² including shower cubicles.
Asia		
High Security Animal Disease Laboratory (HSADL)	India http://www.hsadl.nic.in/	Laboratory has good infrastructural facilities for BSL-4 (animal pathogens); 21 scientists four engineers working with biosafety understanding.

SOURCES: Personal communications: S. Alexandersen, NCFAD, 05/14/2012; P. Daniels, CSIRO, 05/27/2012; T. Mettenleiter, FLI, 05/11/2012; M. Johnson, IAH; 05/15/2012; C. Griot, IVI, 05/15/2012; D.D. Kulkarni, HSADL, 5/16/2012.

^aOther similar facilities exist globally, for example in The Netherlands, South Africa, etc.

^bRoom sizes are net square feet unless indicated otherwise.

The National Institute of Allergy and Infectious Diseases, which is part of NIH, supports 11 university-based laboratories designated as Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases (RCEs). The RCEs conduct research on NIH priority pathogens, some of which are agents of FADs and zoonotic diseases that appear on the OIE lists of animal diseases and top animal disease threats in the United States (see Tables 2-1 and 2-3 in Chapter 2).

Most BSL-4 facilities have a common design that couples dedicated *in vitro* laboratories with adjacent animal rooms, almost always augmented by dedicated rooms for necropsy or animal manipulation. Animal rooms are usually about 200-350 ft² each and are designed to hold rodents, rabbits, or other small animals in racks; each animal room typically can hold two or more racks. The rooms may also hold nonhuman primates, which are often housed in racks of four individual cages (two up, two down), and a single animal room typically can hold 16 or more nonhuman primates. Widely available modern isolation units isolate individual cages and limit air mixing between cages of many smaller laboratory animals, so it is possible to undertake concurrent experiments with different pathogens by using separate animal cages in the same room. “Biobubbles” or “biorooms” can serve the same purpose for nonhuman primates but are less commonly used. Animal rooms used to house nonhuman primates are usually equipped with floor or trench drains with strainers to separate solid waste. They discharge to a central set of reservoirs where waste is sterilized before being discharged into the local sewage system. Floor drains may or may not be in place for animal rooms designed to hold rodents or other small animals.

All solid waste and animal carcasses are sterilized (autoclaved) before leaving the biocontainment laboratory and then usually incinerated. Few of these facilities have large “digesters” capable of processing experimentally infected larger animals. Movement of laboratory animals into biocontainment laboratories often involves the use of elevators and passage through open hallways and loading docks. Waste, animal cages, and bedding are sterilized in double-door autoclaves as the material leaves the laboratory. Equipment and other implements can also be decontaminated in an air lock in which a gas (formaldehyde) or vapor (hydrogen peroxide) is used to fumigate the items. Materials that have been autoclaved or fumigated are then usually cleaned and prepared for reuse at a central facility, often in the laboratory complex.

The handling of agriculturally important animals in existing BSL-4 facilities is challenging but not impossible, although no such facility in the United States is designated as ABSL-4 for large animals. Some facilities are exploring the use of miniature goats or pigs for experimental infection with agriculturally important BSL-4 pathogens, such as Crimean-Congo hemorrhagic fever, Nipah, and Hendra viruses. There are many challenges in conducting such experiments,

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including movement of animals from the supplier into the biocontainment laboratory, animal husbandry and waste management during experimentation, manipulation of large animals in the BSL-4 environment, necropsy procedures, and decontamination of animal carcasses after experimental infection. Those challenges are more fully discussed below.

Choice of Animals

Miniature goats, pigs, young lambs, and perhaps miniature horses could be used for experimental infections in existing BSL-4 facilities in the United States. Larger animals, such as horses and cattle, would present major hurdles and are probably not practical apart from true emergency conditions. The number of individual animals able to be tested at a given time will be small, and this could make it difficult to demonstrate statistically significant results. Special equipment for safe handling of any large animals would have to be procured and installed.

Delivery of Animals

Many existing BSL-4 laboratories are not on the ground level of the buildings that house them. Therefore, animals would need to be moved from a transport vehicle to a biocontainment facility by using existing delivery docks, hallways, and elevators that were not designed for movement of large animals. That problem could be overcome by using crates or other containers for some species and restricting access while animals are being moved.

Animal Husbandry

Animal husbandry is likely to be one of the most challenging aspects of the use of domestic animals in existing biocontainment facilities. Special flooring will be needed to allow efficient waste removal and to provide adequate footing for and protection of hooved animals. Individual corrals can be purchased and installed, or animals can be group-housed in a designated portion of an animal room. Special arrangements will be required for feed and water.

Monitoring Animals

Individual animals can be monitored for vital signs, such as body temperature, with implanted sensors and telemetry. However, direct handling of individual animals for inoculation or to obtain periodic blood samples or other specimens would require the installation of appropriate constraint devices and their use by trained personnel to facilitate the safe handling of the animals during such manipulations.

Necropsy and Carcass Disposal

Most necropsy facilities that are now in place are designed to handle laboratory animals that are the size of nonhuman primates or smaller. Special adaptations might be required to process larger animals, and preparation of carcasses to ensure sterilization on completion of studies will be difficult. Disposal of larger animals after sterilization would require specialized large incinerators that may not be locally available.

Institutional Oversight

All animal experimentation must be reviewed and approved by an institutional animal care and use committee, and the handling of dangerous pathogens must be cleared by an institutional biosafety committee. Those committees ensure that work to be done meets all existing national standards and that it can be accomplished safely and securely. In most instances, the institutions will not have had experience in handling large livestock species, particularly those being experimentally infected with infectious agents. Convincing the committees that domestic animals can be manipulated safely and securely under humane conditions in facilities adapted to accommodate large animals will require careful planning, effective leadership, and a strong partnership between the scientific investigators and the laboratory animal resources team.

International Resources

BSL-4 laboratories outside the United States that have the capacity to handle large animals are shown in Table 3-2. Each facility has the ability to handle large domestic animals and some of these laboratories have experience working with agents that are not currently in the United States but are of research interest and could be newly introduced into the country (for example, Hendra and Nipah viruses at the Australian Animal Health Laboratory in Geelong). Depending on the situation when a request is made, they may be willing to collaborate with US scientists to investigate pathogens that require BSL-4 containment. Their primary responsibility is, of course, to their own national governments and domestic needs.

National and international resources and biocontainment infrastructure for addressing the threat of FADs and zoonotic diseases have expanded substantially since 2001. A discussion of some of the requirements and challenges associated with the design and construction of international high-containment laboratories may be found in the report entitled *Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories* (NAS and NRC, 2012). Can components of the ideal system for countering disease threats use these existing resources effectively? The answer is a cautious yes. However, the chal-

allenges in using the highest level of biocontainment space (ABSL-4), particularly for large-animal research and diagnostic development, are not insignificant.

Adaptability and Flexibility for the Future

Technology

Diagnostics, detection, vaccine development, and therapeutics are primary research necessities to maintain US agricultural strength. The scientific and technological needs of the diagnostic and response capability of the United States were outlined in the 2003 National Research Council report *Countering Agricultural Bioterrorism*:

“There are needs and opportunities for aggressive research in both science and technology to improve our ability to prevent, detect, respond to and recover from biological attacks on agricultural plants and animals. The scientific knowledge and the technological developments for protecting plants and animals against naturally occurring or accidentally introduced pests and pathogens constitute a starting point for these efforts—but only a starting point—and there is much more to be done” (p. 67, NRC, 2003).

Knowledge of naturally occurring agents is itself limited, and the landscape is complicated if one considers intentional introduction of existing or novel “synthetic” threat agents. Identification and characterization of existing pathogens continue to accumulate at rates that are increasing dramatically as a result of new technologies, such as next-generation sequencing. In general, diagnostic tests are moving away from antibody-based, single-pathogen laboratory assays toward nucleic acid-based, multiple-pathogen point-of-care tests. None have yet been considered fit for the purpose of diagnosing FADs of livestock (whose prevalence is virtually zero). However, a survey of recent developments in biotechnology suggests that new, effective methods for diagnosing and tracking human diseases are available or on the near horizon, application to companion-animal diseases has already occurred, and further development for diseases of livestock will follow.

Nanotechnology and microfluidics have contributed to the burgeoning of detection technologies. For example, several advances in nucleic acid-based detection devices will allow diagnosis of known infections—even of infection with BSL-3 organisms—in the field or in the local laboratory. Many of the new devices, such as lateral-flow (hand-held or dipstick) assays for using both nucleic acid and immunoassays, lead to complete independence from laboratory instrumentation. Novel variations on the original PCR assay include (among many) loop-mediated isothermal amplification, molecular beacons, multiplexed

assays, twisted intercalating nucleic acid stabilizing molecules, and dA-tail capturing. Simultaneous interrogation of multiple sequences representing multiple bacterial and viral pathogens is provided by such systems as “lab-on-a-chip” designs and DNA-RNA microarrays; originally requiring laboratory access, these multiplex approaches have recently been adapted to lateral-flow platforms for field use.

Nucleic acid-based and antibody-based platforms are most widespread, but direct chemical analysis of organisms with matrix-assisted laser desorption-ionization time of flight mass spectrometry is also possible. Identification is based on protein profiles of bacterial pathogens, viral glycoproteins, or even multiplexed PCR products. Microorganism-based biosensing methods—such as optical, surface plasmon resonance, amperometric, potentiometric, whole-cell, electrochemical, impedimetric, and piezoelectric methods—are being adapted from food-based assays to clinical use.

Despite substantial advances in detection specificity and sensitivity, there is the remaining problem of sample concentration, as discussed above. Early stages of infectious diseases may have few organisms in accessible tissues. For example, early in *Bacillus anthracis* infection, few bacteria are in the bloodstream despite rapid replication because the bacteria are transported into the lymph nodes by dendritic cells (a subset of immune cells involved in early responses to infection) and are not accessible in traditional tissue sampling. By the time a suitable number of bacteria are present for diagnosis, the infection is rampant and usually fatal. Among the solutions to the problem are detection systems that have highly effective concentration methods that have been developed for such diseases as tuberculosis and malaria. Those systems (such as GeneXpert and Determine™ TB-LAM) rely on automation of complex, time-consuming procedures and encase an entire process in sealed cartridges with excellent safety records and reduce the time needed to confirm a diagnosis with high specificity and sensitivity.

Finally, exponential increases in technology innovation are fueled by intense competition among companies and countries that have marked effects on research and development. Figure 3-4 shows the rates of performance improvement in two sets of technologies: recombinant DNA and synthetic biology (including rapid and low-cost DNA sequencing) (Aldrich et al., 2007). For example, revolutionary advances in DNA sequencing methods (next-generation, deep, and massively parallel sequencing) herald a time when tissue samples from infected animals can be subjected to genome sequencing even without the need for isolation of the organism. As of May 13, 2012, the complete DNA sequences of 11,681 prokaryotes and 3,097 viruses had been posted,¹¹ and cost and time for sequencing are decreasing at an unprecedented rate; third-generation (single-molecule) sequencing will undoubtedly further revolutionize the field.

¹¹URL: <http://www.ncbi.nlm.nih.gov/genome/browse/> (accessed May 12, 2012).

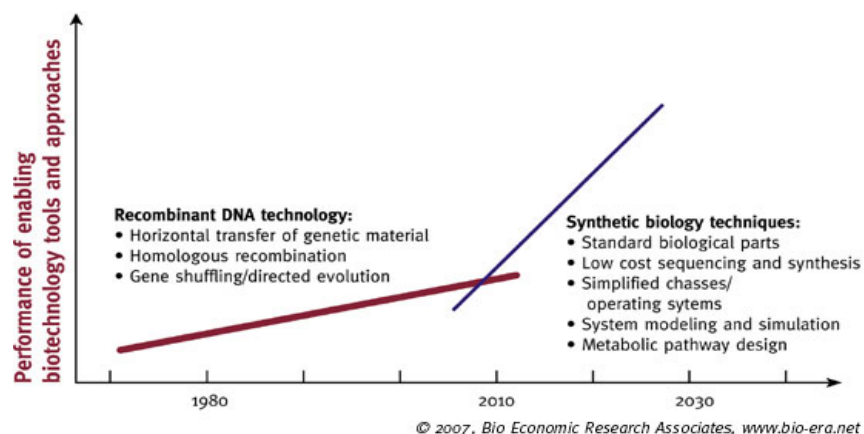


FIGURE 3-4 Rates of performance improvement of recombinant-DNA technology and synthetic biology. SOURCE: Aldrich et al. (2007). Reprinted with permission from Bio Economic Research Associates, LLC (bio-era™). All rights reserved.

High biocontainment will be required in the near term for development, testing and validation of some of those approaches. Eventually, their application to plant and animal health will reduce, but not eliminate, the requirement for specialized laboratory space.

50-Year Lifespan of the Facility

With forethought and proper planning, the design of a facility with a lifespan of 50 years would take into account changes that might take place during the life of the building. They include changes in policy, research priorities, technological developments, societal norms, and global interactions. For example, as noted above, technological advances will shorten the time to diagnosis and expand the array of infections detectable with point-of-care or pen-side assays and reduce laboratory-based testing. Single catastrophic events, such as a massive outbreak or a terrorist event, can change the landscape of a research field and its associated policies.

The decade after the 9/11 and 2001 anthrax attacks in the United States saw unprecedented changes in the regulatory and oversight environment for biomedical research in the United States. The confluence of those two events had substantial effects on laboratory security and safety procedures that limited access to dangerous pathogens and altered research priorities. Similar increased awareness of security and safety issues has occurred on a global level. The new regulatory environment—on both the national and the international levels—is subject to constant adjustment and adaptation, and therefore would require that greater emphasis be placed on the harmonization of regulations: future national

animal agricultural infrastructure and policies would need to be planned with the potential for these changes in mind.

Similarly, societal values and public attitudes related to the welfare of agricultural animals continue to evolve (Blokhuis et al., 2008). Organizations such as OIE are actively promoting the importance of integrating animal health, animal welfare, and food safety. Although the United States currently does not legislate food animal welfare,¹² the European Commission recently adopted a new 4-year strategy (2012-2015) to improve the welfare of animals in the European Union.¹³

Research and development in animal protection will require BSL-3Ag and ABSL-4 for decades to come. Researchers will need to understand disease pathogenesis to develop efficient detection and diagnostic methods or new vaccines. For example, some animals immunized with inactivated foot-and-mouth disease vaccines are still capable of maintaining persistent infection (Kitching, 2002). The variability of foot-and-mouth disease serotypes restricts the use of existing vaccine stocks in an outbreak until a full epidemiological characterization has been carried out and studies to determine whether the vaccine will provide sufficient immunity against the viral outbreak strain have been conducted (Rodriguez and Gay, 2011). Furthermore, if vaccines are used to control an outbreak, the ability to detect infection in vaccinated animals and to differentiate between infected and immunized animals is required if animal products are to be moved within the country and globally. As more is understood about disease progression and virulence determinants in infection, attenuated or recombinant viral vaccines will be produced by using reverse-engineering and other synthetic technologies, with serotype specificity and DIVA properties. Development of such a vaccine is well advanced in the United States and abroad. Those and other novel vaccine-production platforms are essential for rapid response to foot-and-mouth disease outbreaks and will need to be tested in large animals in strict containment. The committee notes that one such foot-and-mouth disease vaccine was licensed recently (June 2012). This vaccine was a product of PIADC and USDA-ARS research in cooperation with DHS and the private sector.¹⁴

Vaccine development for agents that are emerging as high-priority disease threats may also require high biocontainment. Bunyaviruses, such as Crimean-Congo hemorrhagic fever virus and Rift Valley fever virus, are the causative agents of devastating diseases and have an expanding host and geographic range. Investigation of those agents in livestock species is necessary. Recent advances in research methods such as infectious-virus rescue, novel electron microscopic techniques, and high-resolution structural analysis have been ap-

¹²See URL: <http://awic.nal.usda.gov/farm-animals/animal-welfare-audits-and-certification-programs> (accessed May 31, 2012).

¹³See URL: http://ec.europa.eu/food/animal/welfare/actionplan/actionplan_en.htm. (accessed May 31, 2012).

¹⁴ See URL: <http://www.prnewswire.com/news-releases/genvec-announces-conditional-approval-of-fmd-vaccine-for-cattle-157766595.html> (accessed June 29, 2012).

plied to both emerging bunyaviruses and model species (Walter and Barr, 2011). The study of those agents has high priority in view of the lack of vaccines and therapeutics for their treatment and control and requires high biocontainment.

Finally, the committee also recognizes that there are international research efforts to develop vaccination studies that involve no challenge infections of animals with live virus. These studies are critical for the large number of countries recognized by the OIE as “foot-and-mouth disease-free with vaccination” whose foot-and-mouth disease research facilities are unable to use live FMDv for any studies or challenges. Efficacy studies for FMDv would be based solely on the evaluation of immune response elicited by vaccination, as is already happening in the case of foot-and-mouth disease vaccines manufactured in South America under guidelines of the Pan-American Foot-and-Mouth Disease Center (PANAFTOSA). It is expected that efforts to develop alternative efficacy studies of new vaccines without experimental challenge infections of live animals will continue to evolve given regulatory and societal pressures to limit the number of animals used in infectious disease research, with an obvious impact on the capacity needed for animal studies in high biocontainment.

SUMMARY

Despite the marked expansion of high-biocontainment space in the United States since 2001, there remains no national ABSL-4 large-animal facility. Similarly, although BSL-3Ag containment space has expanded through construction of several new facilities (for example, the Biosecurity Research Institute and the National Animal Disease Center), the facilities at PIADC dedicated to FADs are dated and increasingly cost-inefficient. Thus, there is a critical national need for a dedicated facility that has modern BSL-3Ag and ABSL-4 large-animal capabilities. It would serve as the hub of the national strategy for the detection of and response to any incursion of an FAD. It would also be used for the study of infectious diseases of public-health importance in which livestock serve as key reservoir or amplifying hosts.

US programs for detection of and response to FADs (those proposed to be located at the NBAF) would need to interface with similar activities and programs of the National Biodefense Analysis and Countermeasures Center, the Centers for Disease Control and Prevention, the US Army Medical Research Institute for Infectious Diseases, USDA, NIH, and academic and state institutions to maximize efficiency and intellectual resources through interdisciplinary research that crosses traditional agency boundaries. Such interagency working relationships may have challenges, but would be essential for maximizing the use of the NBAF as well as other existing BSL-3Ag, BSL-4 and ABSL-4 laboratories in the United States and the skilled workforce they employ. The rapidly evolving nature of disease threats confronting the animal industries of the United States and the technologies available to detect and respond to them demand a flexible and nimble strategy for programmatic and facility design. With

that background, in Chapter 4 the committee considers in more detail the three options presented in its statement of task: constructing the NBAF as currently designed, scaling back the size and scope of the proposed NBAF, and maintaining the current PIADC and leveraging US capability and capacity through international laboratories that have ABSL-4 large-animal space.

REFERENCES

- Aldrich, S.C., J. Newcomb, and R. Carlson. 2007. Figure 1-2. An inflection point for biological technology . In *Genome Synthesis and Design Futures: Implications for the US Economy*. Bio-era.net [online]. Available: <http://www.bio-era.net/reports/genome.html> (accessed June 5, 2012).
- Baker, M.G., and D.P. Fidler. 2006. Global public health surveillance under new international health regulations. *Emerging Infectious Disease* 12(7):1058-1065.
- Berns, K.I., A. Casadevall, M.L. Cohen, S. Ehrlich, L.W. Enquist, J.P. Fitch, D.R. Franz, C.M. Fraser-Liggett, C.M. Grant, M.J. Imperiale, J. Kanabrocki, P.S. Keim, S.M. Lemon, S.B. Levy, J.R. Lumpkin, J.F. Miller, R. Murch, M.E. Nance, M.T. Osterholm, D.A. Relman, J.A. Roth, and A. Vidaver. 2012. Adaptations of avian flu virus are a cause for concern. *Science* 335(6069):660-661.
- Blokhuis, H.J., L.J. Keeling, A. Gavinelli, and J. Serratosa. 2008. Animal welfare's impact on the food chain. *Trends in Food Science and Technology* 19 (suppl. 1):S79-S87.
- Brownlie, J., C. Peckham, J. Waage, M. Woolhouse, C. Lyall, L. Meagher, J. Tait, M. Baylis, and A. Nicoll. 2006. *Foresight. Infectious Diseases: Preparing for the Future. Future Threats*. London: Office of Science and Innovation [online]. Available: <http://www.bis.gov.uk/assets/foresight/docs/infectious-diseases/t1.pdf> (accessed June 4, 2012).
- CDC (Centers for Disease Control and Prevention). 2009. *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, 5th Ed. (CDC) 21-1112. [online]. Available: <http://www.cdc.gov/biosafety/publications/bmb15/BMBL.pdf> (accessed June 5, 2012).
- CNA. 2011. *Enhancing Ag Resiliency: The Agricultural Industry Perspective of Utilizing Agricultural Screening Tools*. Report from the Agricultural Screening Tools Workshop, April 2011, Washington D.C. College Station, TX: National Center for Foreign Animal and Zoonotic Disease Defense, Texas A&M University [online]. Available; <http://fazd.tamu.edu/files/2011/06/ASTII-Report-FINAL.pdf> (accessed June 5, 2012).
- Enserink, M., and J. Cohen. 2012. One H5N1 paper finally goes to press; Second greenlighted. *Science* 336(6081):529-530.
- Fidler, D.P. 2005. From international sanitary conventions to global health security: The new international health regulations. *Chinese Journal of International Law* 4(2):325-392.
- IOM (Institute of Medicine). 2003. *Microbial Threats to Health: Emergence, Detection, and Response*. M.S. Smolinski, M. A. Hamburg, and J. Lederberg, eds. Washington, DC: The National Academies Press.
- IOM and NRC (National Research Council). 2009. *Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases*. G.T. Keusch, M. Pappaioanou, M.C. Gonzalez, K.A. Scott, and P. Tsai, eds. Washington, DC: The National Academies Press.

- Kahn, C.M., and S. Line, eds. 2011. Akabane virus infection. The Merck Veterinary Manual. Whitehouse Station, NJ: Merck [online]. Available: <http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/50804.htm> (accessed June 29, 2012).
- Kitching, R.P. 2002. Identification of foot and mouth disease virus carrier and subclinically infected animals and differentiation from vaccinated animals. *Scientific and Technical Review* 21(3):531-538.
- NAS (National Academy of Sciences) and NRC. 2012. *Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories: Summary of a Workshop*. Washington, DC: The National Academies Press.
- NASDARF (The National Association of State Departments of Agriculture Research Foundation). 2001. *The Animal Health Safeguarding Review: Results and Recommendations*, October 2001 [online]. Available: http://www.aphis.usda.gov/vs/pdf_files/safeguarding.pdf (accessed June 8, 2012).
- NRC (National Research Council). 2003. *Countering Agricultural Bioterrorism*. Washington, DC: The National Academies Press.
- OIE (World Organization for Animal Health). 2010. Chapter 1.2 Criteria for Listing Diseases Article 1.2.1. Terrestrial Animal Health Code 2010 [online]. Available: http://web.oie.int/eng/normes/mcode/en_chapitre_1.1.2.pdf (accessed June 1, 2012).
- Rodriguez, L.L., and C.G. Gay. 2011. Development of vaccines toward the global control and eradication of foot-and-mouth disease. *Expert Review of Vaccines* 10(3):377-387.
- USDA (US Department of Agriculture). 2012. *USDA Responses and Supporting Materials to the Questions Sent by the Committee*. April 27, 2012.
- USDA-APHIS (US Department of Agriculture, Animal and Plant Health Inspection Service). 2012. *National Animal Health Laboratory Network (NAHLN)* [online]. Available: http://www.aphis.usda.gov/animal_health/nahln/content/wp_c_map_disp.php?lab=all_labs_disease_designations (accessed June 5, 2012).
- Walter, C.T., and J.N. Barr. 2011. Recent advances in the molecular and cellular biology of bunyaviruses. *Journal of General Virology* 92:2467-2484.
- WHO (World Health Organization). 2007. *International Health Regulations (2005): Areas of Work for Implementation*. WHO/CDS/EPR/IHR/2007.1. France, Lyon: World Health Organization [online]. Available: <http://www.who.int/ihr/finalversion9Nov07.pdf> (accessed June 4, 2012).

4

Analysis and Conclusions about Three Approaches for Providing US Infrastructure to Counter Foreign Animal Disease and Zoonotic Disease Threats

As part of its statement of task, the committee was asked to analyze three options for achieving the infrastructure needed to address threats posed by foreign animal diseases (FADs) and zoonotic diseases. Those options are building the National Bio- and Agro-Defense Facility (NBAF) as currently designed, building a version of the NBAF of reduced size and scope to be described by the committee, and maintaining the Plum Island Animal Disease Center (PIADC) in conjunction with obtaining biosafety level 4 (BSL-4) livestock capacity through partnerships with foreign laboratories. The committee analyzed the options with regard to how they might achieve an overall integrated US system that incorporates the critical core functions of disease surveillance, diagnostics, outbreak response and recovery, research and development, and workforce training described earlier in this report, as well as expected future needs (see Chapter 3). Successful implementation of those critical systemwide functions requires practical infrastructure and laboratory capacity. This chapter provides a brief history of previous long-term planning efforts, which demonstrates that many of the same issues have plagued the US system for addressing FAD and zoonotic disease threats for many years. The history provides context for the committee's current analysis. This is followed by the committee's assessment of what the needed research and diagnostic laboratory infrastructure would include, regardless of the option considered for the central laboratory facility. In subsequent sections, the committee discusses the three options and assesses how they address capacity needs, such factors as relative costs, and other considerations.

PREVIOUS LONG-TERM PLANNING EFFORTS

In 1983, the National Research Council released the report *Long-Term Planning for Research and Diagnosis to Protect U.S. Agriculture from Foreign Animal Diseases and Ectoparasites* (NRC, 1983). The study was requested in 1982 by the US Department of Agriculture (USDA) to “assess the current state of the USDA effort on FAD&E [foreign animal diseases and ectoparasites] diagnosis and research; assess, for three 10-year increments, current and projected technology of biological containment; and assist USDA in planning, in three 10-year increments, for research on and diagnosis of all FAD&E of livestock and poultry” (NRC, 1983).

The deliberations and recommendations in the 1983 report have a strong resonance with the questions posed to the current National Research Council committee 30 years later. Main themes of the 1983 report were that the facilities at PIADC for conducting FAD and ectoparasite research and diagnostics were obsolete and that the United States needed to contemplate several options to maintain strong protection of our animal industries and economy in the face of a threat of FADs and ectoparasites. In addition to recommendations that addressed the need for long-term research planning and coordination, the 1983 NRC report said that

- “USDA should increase coordination [of FAD&E activities] with other federal agencies and foreign institutions” (NRC, 1983).
- “USDA should establish a system of laboratories and university-based collaborative research centers for investigation, research, and diagnosis of domestic and foreign animal diseases and ectoparasites” (NRC, 1983).
- “As soon as possible, USDA should proceed with construction of a new, highly secure mainland laboratory to succeed PIADC as USDA’s principal center for research on exotic airborne and fomites-transmitted non-avian animal diseases” (NRC, 1983).

The report further suggested the need for BSL-4 capabilities and proximity to a major airport and a major university campus to ensure ready access and a supportive scientific environment. It also suggested that PIADC be maintained for large-animal challenge and vaccine studies in view of the legal restrictions on working with foot-and-mouth disease virus (FMDv) on the mainland.

Eleven years later, in 1994, USDA appointed a *Task Force on Biocontainment Facilities for Foreign Animal Disease Research and Diagnostic Activities* (USDA, 1994) to consider two issues: the progress made in the preceding decade in new technology development and use for handling FAD agents since the publication of the 1983 National Research Council report, and the current status of and physical requirements for large-animal biocontainment facilities for conducting FAD research and diagnostic activities in the near term and the long-range future.

Regarding progress on research and diagnostic technologies, the 1994 task force indicated that in vitro modern technologies were available for studying FAD pathogens but that the use of in vivo studies was still needed for

- The isolation of etiological agents to activate federal programs for disease control and eradication, particularly in the case of new emerging pathogens that could not be isolated in vitro.
 - Conducting pathogenesis studies and proving Koch’s postulates.
 - Continuing to train state and federal veterinarians in the recognition of FADs by using live-animal reproduction of key FADs.

Those justifications of a facility with the capability for live-animal studies under strict biocontainment remain highly relevant today and were previously discussed in Chapters 2 and 3 of this report.

Regarding the status of facilities to conduct FAD research and diagnostic activities, the 1994 task force found that despite the recommendations of the 1983 National Research Council report, the PIADC facilities remained badly in need of upgrading to achieve world-class designation. In 1994, an estimated \$80-100 million was needed for repairs and upgrades. There have been periodic upgrades and renovations of PIADC since the 1994 report, but the general state of PIADC in 2012 has not changed. The task force also pointed out that several existing or planned facilities on university campuses may be capable of FAD research and diagnostic activities but that many of them may have obsolete technologies, may be underused, or have not been adequately maintained. As previously discussed in Chapter 3, however, the status of university and federal facilities in 2012 is substantially different from that in 1994. Finally, the 1994 task force offered nine potential options regarding the future of PIADC, categorized into three groups as listed below. The reader is referred to that report for additional information on options that are not presented in detail below.

Group One—Retain Plum Island Operations

Options 1-4: Several possibilities for achieving this recommendation were presented, but they are not central to this report.

Group Two—Relocate Plum Island Operations to a Mainland Site

Option 5: Construct new mainland FAD facilities. “Request an upfront, lump-sum appropriation, and construct new FAD facilities at a mainland site. Continue to use existing FAD facilities on Plum Island until construction is completed on the mainland. Continue to conduct domestic disease and selected FAD work in separate mainland facilities” (USDA, 1994).

Option 6: Construct new mainland facilities; consolidate domestic and FAD work. “Request an upfront, lump-sum appropriation, and construct new FAD facilities at a mainland site (for both domestic and FAD work). Continue to use

the existing island and mainland facilities until construction is completed on the mainland. Consolidate both foreign and domestic animal disease work at the new mainland facilities” (USDA, 1994). (The completion of the National Centers for Animal Health in Ames, Iowa, now supersedes the consideration of consolidation of domestic and FAD facilities in a single facility.)

Option 7: Upgrade Plum Island for foot-and-mouth disease work only; move other work to the mainland. “Request partial appropriations each year as required to upgrade/repair the Plum Island facilities, but [in view of the legal restrictions on working with foot-and-mouth disease virus on the mainland] only to the extent needed to conduct live-animal FMD challenge work. Relocate all other FAD activities to existing mainland sites” (USDA, 1994), such as the National Animal Disease Center, the National Veterinary Services Laboratories, the Southeast Poultry Research Laboratory, and the Arthropod-Borne Animal Diseases Research Laboratory.

Group Three—Unacceptable Options

Option 8: Upgrade Plum Island for foot-and-mouth disease work; contract other FAD work. “[Maintain] a small Plum Island unit for FMD studies and [contract] all other FAD activities with universities on the mainland. This option was discarded because it would have afforded insufficient control and oversight to ARS and APHIS [the USDA Agricultural Research Service (ARS) and Animal and Plant Health Inspection Service (APHIS)], required large expenses for renovated or new university containment facilities, and continued expenditures at Plum Island” (USDA, 1994). (But with the construction of multiple new bio-containment facilities throughout the United States since the 1994 report was issued, the present committee views that this option should no longer be considered unacceptable, as discussed further below.)

Option 9: Have ARS and APHIS seek independent decision-making and funding. “Option 9 would have isolated ARS and APHIS, setting each agency off on its own to seek independent answers, decision making, and funding. This option was discarded because it would have meant less control and oversight of FAD work by ARS and APHIS, and it would have led to higher overall costs” (USDA, 1994).

Additional USDA, Department of Homeland Security (DHS), and National Research Council reports echoed many of those issues, including concerns that the PIADC facilities were at the end of their lifespan and needed modernization and other upgrades and that a facility with BSL-4 large-animal capabilities was needed (USDA, 1999; NRC, 2005; DHS, 2007a,b, 2008a; CRS, 2008; 74 Federal Register, 2009).

Previous National Research Council reports provide a historical perspective for consideration of the three options specified in the present committee's statement of task. However, the committee's deliberations were conducted independently of previous report recommendations to ensure that the current context of disease threats, the ideal infrastructure to counter the threats, the technology of "today and tomorrow", and the current US and global assets available for countering disease threats informed the current study. Nevertheless, previous recommendations remain, in part, as relevant today as they were in 1983, 1994, and later. The following sections discuss the three options the committee was asked to address with respect to capacity and capabilities, advantages and liabilities, relative costs, and other considerations.

**THE LABORATORY INFRASTRUCTURE NEEDED
FOR A FOREIGN ANIMAL DISEASE AND ZOOONOTIC
DISEASE RESEARCH AND DIAGNOSTIC FACILITY,
REGARDLESS OF LOCATION AND SIZE**

A US system to address the potential threats posed by FADs and zoonotic diseases effectively must include the ability to conduct research and diagnostic procedures, provide training to support a competent and prepared workforce, and include specialized facilities for handling particular pathogens and for conducting experiments in large animals. The facility and program components of the ideal system are depicted in Figure 3-1, and a more detailed description of the laboratory infrastructure that would be required to meet those objectives is described below. The numbers beside the headings below correspond to the numbers in Figure 4-1.

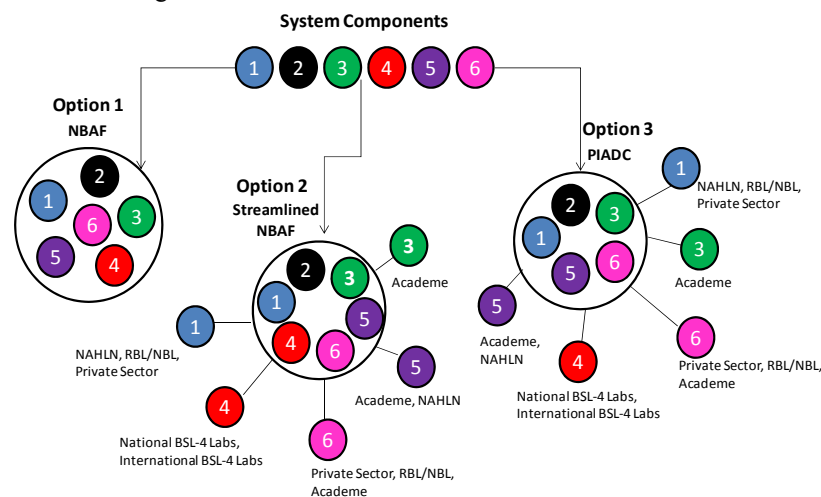


FIGURE 4-1 Comparison of the three options analyzed by the committee with the components of an ideal laboratory infrastructure. The examples given are for illustration only

and are not meant to be inclusive. See Table 4-1 for more detail. NOTE: 1 = diagnostics, 2 = research on foot-and-mouth disease, 3 = research on non- foot-and-mouth disease FADs and zoonotic diseases in BSL-3Ag facilities, 4 = special pathogen activities in ABSL-4 and BSL-4 facilities, 5 = teaching and training, 6 = vaccine development. NAHLN = National Animal Health Laboratory Network; RBL/NBL = Regional Biocontainment Laboratories and National Biocontainment Laboratories.

Diagnostics (1)

Laboratory infrastructure for the isolation, identification, and diagnosis of FADs and zoonotic diseases is needed at several levels of biocontainment. In vitro diagnostic work with inactivated pathogens or pathogen components may be conducted with BSL-2 containment. Such work would include identification of an agent with nucleic acid-based methods, such as the polymerase chain reaction (PCR); detection of antigens with antibody-based methods, such as the enzyme-linked immunosorbent assay (ELISA); or characterization of host immune responses to key agent antigens. In addition, reference reagent preparation (when working with inactivated pathogen material), proficiency-testing panels, and other activities related to support for state-based testing laboratories can be conducted with BSL-2 containment. In vitro diagnostic work and the isolation of live pathogens may generally be conducted in space at BSL-2, BSL-3, or BSL-4 levels. BSL-3Ag space is generally not required for working in vitro.¹

Research on Foot-and-Mouth Disease (2)

Ease of transmission and the potential for large economic effects of an outbreak of foot-and-mouth disease make it a disease of special consideration. Active research is ongoing to develop diagnostics for and vaccines against foot-and-mouth disease virus (FMDv) strains. Currently, foot-and-mouth disease research can be conducted in only one US facility: PIADC, off the US mainland. Because of the special circumstances and restrictions surrounding foot-and-mouth disease research, the committee considers it separately. In vitro work on foot-and-mouth disease is conducted at BSL-3E level, and in vivo experiments with FMDv are conducted at the BSL-3Ag level.

¹The 5th edition of *Biosafety in Microbiological and Biomedical Laboratories* supports conducting in vitro work with animal pathogens at the BSL-3 level, restricting the use of BSL-3Ag to only situations in which particular FAD agents are used in infectivity studies and when animals are loose in an isolation room (in which the walls of the room itself form the primary containment barrier). Those agents are African swine fever virus, lumpy skin disease virus, highly pathogenic avian influenza virus, *Mycoplasma mycoides* subsp. *mycoides* (small colony type), *Mycoplasma capricolum*, Newcastle disease virus (velogenic strains), Peste des petits ruminants virus (plague of small ruminants), Rift Valley fever virus, rinderpest virus, classical swine fever virus, and foot-and-mouth disease virus (CDC, 2009).

Research on Foreign Animal Diseases and Zoonotic Diseases in BSL-3Ag Facilities (3)

The necessary laboratory infrastructure for *in vivo* experiments on many FADs and zoonotic diseases includes animal holding facilities for microbiological, immunological, and pathogenesis studies at BSL-3Ag and ABSL-3E level containment. Experiments at ABSL-3E can occur where animals are housed in cages. BSL-3Ag containment is required for *in vivo* experiments on large animals that must be housed directly in an isolation room. In addition, the capability to conduct *in vivo* studies of some pathogens associated with arthropod vectors requires BSL-3Ag facilities. A separate set of guidelines, known as Arthropod Containment Levels, is used to define the biocontainment needed for safe manipulation of live arthropods (ASTMH, 2003).

Special Pathogen Activities in ABSL-4 and BSL-4 Facilities (4)

Research with some pathogens can be conducted only at BSL-4 or ABSL-4 containment. Those pathogens currently include hemorrhagic fever viruses (such as Crimean-Congo hemorrhagic fever virus) and the new genus of Henipavirus in the Paramyxoviridae family (Nipah and Hendra viruses).² BSL-4 laboratory capabilities are also needed more generally as part of an effective US system to counter FAD and zoonotic disease threats because of the possible emergence of new highly contagious zoonotic pathogens. In particular, BSL-4 and ABSL-4 will be required for initial work on newly emerging or unknown diseases in order to provide protection to researchers from unknown biological hazards until these can be more fully characterized. The required laboratory capacity includes the ability to undertake *in vitro* microbiological research, such as propagation

²The primary reservoir for Henipaviruses is bats of the Pteropus family, whose range includes the eastern coastal areas of Australia, Southeast Asia, and South Asia. Hendra virus was first recognized in 1994, and outbreaks have occurred only in Australia; Nipah virus was first recognized in 1998, and outbreaks have occurred in Malaysia, Bangladesh, and India. The probability of a natural introduction and establishment of either Nipah virus or Hendra virus in the United States is small, and an outbreak in animals or people is unlikely to lead to establishment of either one of these two viruses in the Western Hemisphere, because of the absence of the primary vector or reservoir bat species. However, capabilities to work with viruses that require BSL-4 and ABSL-4 conditions, such as Hendra virus and Nipah virus, are desirable for counter-bioterrorism and for potential vaccine development, primarily for human or animal use in endemic areas. Active research on Nipah and Hendra viruses is under way at BSL-4 facilities in the United States (*in vitro* and *in vivo*) and in Australia and Canada (*in vitro* and in livestock animal models), and active research on vaccines with cloned proteins is going on at several BSL-2/BSL-3 laboratories in the United States and abroad.

and basic characterization of pathogens, at the BSL-4 level.³ Facilities for in vivo experimentation in animal systems are also required at the BSL-4 level, as is a necropsy room for postmortem examinations on both small and large animals. ABSL-4 facilities are required for in vivo experiments.

Teaching and Training (5)

The facilities necessary to train a prepared workforce include teaching classrooms outside primary containment and laboratory facilities at several containment levels. Animal holding facilities for the in vivo demonstration of clinical and pathological manifestations of selected diseases in small animals housed with primary containment cages require ABSL-3E or ABSL-3.⁴ Animal holding facilities for in vivo demonstration in larger animals requires BSL-3Ag. A necropsy room for training and demonstration purposes is required at the BSL-3Ag level.

Vaccine Development (6)

Laboratory experiments as part of vaccine or other product development for FADs and zoonotic diseases (except for special pathogens) will require BSL-3 and BSL-3E facilities. In vivo pathogen challenge and vaccine efficacy experiments in large animals will require BSL-3Ag.

Examination of the Three Options

With those requirements providing a framework, the committee turned to a fuller discussion of the three options presented in the statement of task. The options are depicted in Figure 4-1, with demonstration of one example of several possible configurations for Options 2 and 3, and presented in greater detail with multiple examples in Table 4-1.

³As noted earlier, BSL-4 containment is not required for basic diagnostic work with inactivated pathogens and non-replicating methodologies, such as PCR and other nucleic acid detection procedures.

⁴For example, work with avian influenza in chickens housed in ventilated cages at the ABSL-3 level.

TABLE 4-1 Possible Location of Key Laboratory-Based Components of the Ideal System for Countering Foreign Animal Disease and Zoonotic Disease Threats

Components	NBAF as Designed	NBAF-Streamlined	NAHLN	RBL/NBL BSL-3 Laboratories	BSL-3Ag/Academe	Private Sector Laboratories	National BSL-4 Laboratories	International BSL-4 Laboratories
Diagnostics								
In vitro—nonviable/performance	X	X	X					
In vitro—nonviable/development	X	O	X	X		X		
In vitro—viable agents/performance	X	X						
In vitro—viable agents/development	X	O		X	X			
In vivo diagnostics (animal inoculations)	X	X			O		O	
National reference function	X	X						
Foot-and-mouth disease virus research								
In vitro activities	X	X						
In vivo activities (including training)	X	X						
FAD research (non-foot-and-mouth disease)								
In vitro BSL-3/BSL-3E	X	X			O	O		
In vivo BSL-3Ag	X	X			O			

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(Continued)

TABLE 4-1 Continued

Components	NBAF as Designed	NBAF-Streamlined	NAHLN	RBL/NBL BSL-3 Laboratories	BSL-3Ag Academe	Private Sector Laboratories	National BSL-4 Laboratories	International BSL-4 Laboratories
Zoonotic disease research								
BSL-3/BSL-3E	X	O		X			X	
BSL-4	X	X					X	X
Training using animals								
FADs except foot-and-mouth disease	X	O	O		X			
Vaccine development								
Development of principle	X	O		O	O	O		
Proof of principle	X	O		O	O	O		
Scale-up development	X					X		
Animal efficacy studies	X	X			O			

NOTE: X = principal location, O = optional location.

Figure 4-1 and Table 4-1 focus on potential US partnerships to address key laboratory components of an ideal system to address FAD and zoonotic disease threats, with the exception of international BSL-4 laboratory capacity, since this was included in the committee's task as part of option 3. However, the committee also notes that international collaborations can be developed to contribute to laboratory infrastructure at other biosafety levels, such as BSL-3Ag.

ANALYSIS OF OPTION 1: THE PROPOSED NATIONAL BIO- AND AGRO-DEFENSE FACILITY AS CURRENTLY DESIGNED

The Capacity and Capabilities of the Proposed National Bio- and Agro-Defense Facility

The NBAF is envisioned as a modern laboratory resource for consolidating the research, diagnostic, and training missions of DHS and USDA (specifically, APHIS and ARS) in a single facility. Activities that would be conducted in the proposed NBAF include studies of high-consequence FADs and zoonotic diseases that pose a threat to the US animal industry—such as foot-and-mouth disease, African swine fever (ASF), and classical swine fever (CSF)—and studies of emerging zoonotic and high-threat exotic agents that affect livestock and require high containment at the ABSL-4 level. According to DHS's *Updated Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment* (DHS, 2012a), the NBAF, once operational, would support or provide

- Basic and applied research on transboundary (foreign), emerging, and zoonotic diseases.
- Enhanced ability to perform laboratory diagnostic detection of and respond to FADs and zoonotic diseases.
- Expanded and dedicated space for development of vaccines and other countermeasures.
- Training facilities for animal health specialists to improve US capability of detecting and responding to FADs of high consequence.

The proposed NBAF campus, with an area of 715,000 gross ft², would provide infrastructure needed by DHS and USDA to meet their program requirements and would provide supporting facilities (DHS, 2012b). In addition to current mission needs, DHS, APHIS, and ARS propose to expand their relevant research and development activities and have designed NBAF with that in mind. ARS proposes to expand its programs on emerging and zoonotic pathogens beyond FMDv, CSF virus, and ASF virus and to expand its research program on vector-borne diseases. APHIS anticipates expanding its activities related to diagnostic services and reference materials for emerging and zoonotic diseases and to enhance FAD diagnostics and training. DHS anticipates expanding its research programs on the development of new foot-and-mouth disease vaccines

and adding research on countermeasures for other high-priority FADs and zoonotic diseases (Colby, 2012; Kappes, 2012; Lautner, 2012). (Budgets for operational expenses of the NBAF were not part of the charge of this study. The committee notes that the anticipated expanded activities must be accompanied by a corresponding operational budget increase to each agency, however no data on research or diagnostic budgets for expanded programs were received.)

Much of the space in the NBAF main laboratory would be occupied by the biocontainment zone, which includes BSL-3E, BSL-3E Special Procedures, BSL-3Ag, BSL-4, ABSL-4 laboratories, and supporting facilities. The BSL-4 space would be suitable for large-animal research and would include space for ABSL-4 large-animal holding and ABSL-4 large-animal necropsy facilities. Table 4-2 summarizes the features of the proposed NBAF and the purpose of each feature. Table 4-3 summarizes the animal-holding capabilities. According to DHS, the total projected annual animal counts for the facility, based on 70% space use, is “approximately 1,233 animals with a distribution of 519 bovine, 491 swine, 180 mice, 25 rabbits, 8 equine, 6 guinea pigs, [and] 4 goats” (DHS, 2012b).

Analysis of Option 1: Laboratory Capacity

The NBAF as currently designed is meant to serve as a single facility to span the array of required biosafety containment levels and to include pilot-scale vaccine-development production capabilities, which would enable it to include all of the types of laboratory capability and capacity required for an ideal system as described above.

According to DHS, ARS, and APHIS, the agencies undertook a design review process to “right-size” the facility to ensure that space would align with agency mission needs and minimize substantial excess capacity. As part of this process, the net BSL-4 space was reduced by 2,025 ft² and the net BSL-3Ag and BSL-3E space by 31,466 ft² from the initial design phase in 2009 to the 65% design phase in 2011. The projected animal-room use chart provided by the agencies anticipates about 70% average occupancy, with the estimated occupancy of different types of rooms being about 50-90% (DHS, 2012b).

The NBAF has been designed with the ideal system in mind so that it could be self-sufficient. The committee agrees that the proposed facility (based on the 65% design phase plans) would provide the needed capability and capacity to meet US needs. The committee also notes that the Western Hemisphere lacks sufficient ABSL-4 large-animal capacity; the only laboratory in North and South America is in Winnipeg, Canada and this facility has very little large-animal space. That is striking when one considers that countries such as the UK, Germany, and Switzerland, perhaps recognizing that zoonotic disease knows no boundaries, have each invested in BSL-4 space within their borders. There are also potential opportunities for some types of capacity to be provided through partnerships with other state, federal, and university laboratories in the United

States. That option is discussed in more detail under Option 2. Although the NBAF is designed to provide the range of required laboratory capabilities in a single facility, if it were to be operated in a stand-alone fashion without drawing on the nation's physical and intellectual capital, it would not meet the needs of an ideal US system to address FADs and zoonotic disease threats. However, the committee notes that building the NBAF as designed does not preclude the NBAF from functioning as part of such an integrated and collaborative system.

TABLE 4-2 Summary of NBAF Capacity and Capabilities

Feature and Total Area	Purpose
BSL-2 space (19,402 gross ft ² ; 9,701 net ft ²)	Allowing improved throughput and multiagency use; examination and processing of FBI samples (to be passed into BSL-3E or held at BSL-2 for testing at Ames if found to be foot-and-mouth disease-free); housing of arthropods procured from vendors and other laboratories or rearing of arthropods; insect-vector research; space for packaging and shipping reagents to collaborators
BSL-3Ag laboratories (animal holding rooms, necropsy rooms, support services functions, including laundry, loading dock, decontamination service, office operations) (215,700 gross ft ² ; 53,925 net ft ²)	Allowing additional parallel vaccine trials for FADs and zoonotic diseases; shared common core laboratories to provide optimal flexibility and efficiency of space; animal holding rooms to house various species of different sizes in BSL-3Ag environment; two necropsy rooms—one dedicated to research and diagnostic programs, the other to FAD training program
BSL-3E laboratories, including BSL-3E Special Procedures laboratory (149,840 gross ft ² ; 37,460 net ft ²)	Allowing associated laboratory research and diagnostic work; special-procedures laboratory—core facilities for centrifugation and other aerosol-generating activities to support BSL-3Ag and BSL-4 research and includes additional level of high-efficiency particulate air filtration
BSL-4 animal and laboratory space (53,624 gross ft ² ; 13,406 net ft ²)	Allowing USDA-ARS to conduct FAD and zoonotic disease research; allowing USDA-APHIS to perform diagnostic test development and validation, reagent production, and diagnostic specimen testing; allowing DHS (in partnership with USDA-ARS and USDA-APHIS) to develop countermeasures for veterinary and other high-consequence zoonotic diseases
BSL-2 biotechnology development module (pilot production facility) (41,955 gross ft ² ; 8,300 net ft ²)	Allowing manufacture of materials for conducting and supporting efficacy studies to provide preliminary toxicology or general safety data for manufacture of larger volume of early clinical-phase materials

SOURCE: DHS, 2012b; Johnson and Barrett, 2012.

TABLE 4-3 Numbers and Types of Large Animals that can be Handled in the Proposed NBAF Animal Rooms

Room Type ^a	No. Rooms	Anticipated Animal Capacity per Room
BSL-3Ag A	4	Cattle 2 @ <1,430 lb or 4 @ <770 lb or 6 @ <440 lb; OR swine 16 @ <220 lb; OR sheep 18 @ <110 lb
BSL-3Ag A2 (10 x 12 ft)	15	Cattle 2 @ <770 lb or 3 @ <440 lb; OR swine 6 @ <220 lb; OR sheep 8 @ <110 lb
BSL-3Ag A2 (12 x 12 ft)	20	Cattle 1 @ <1,430 lb or 2 @ <770 lb or 3 @ <440 lb; OR swine 8 @ <220 lb; OR sheep 9 @ <110 lb
BSL-3Ag A3	1	Cattle 2 @ <1,430 lb or 4 @ <770 lb or 6 @ <440 lb; OR swine 16 @ <220 lb; OR sheep 18 @ <110 lb
BSL-3Ag B	3	Cattle 4 @ <1,430 lb or 8 @ <730 lb or 12 @ <440 lb; OR swine 32 @ <220 lb; OR sheep 36 @ <110 lb
BSL-3Ag C	2	Cattle 9 @ <1,430 lb or 16 @ <770 lb or 24 @ <440 lb; OR swine 48 @ <220 lb; OR sheep 57 @ <110 lb
BSL-3Ag D	1	Cattle 12 @ <1,430 lb or 21 @ <770 lb or 32 @ <440 lb
BSL-4	2 (can also be used as BSL-3Ag swing space)	Equine animals 2 @ <1,440 lb; OR cattle 2 @ <1,440 lb or 4 @ <770 lb or 6 @ <440 lb; OR swine 8+ @ <110 lb or 16+ @ <55 lb; OR sheep 8+ @ <110 lb or 16+ @ <55 lb
Additional small- animal rooms	—	Mice, rabbits, guinea pigs, and so on

SOURCE: DHS, 2012b.

^aRoom designations A, A2, A3, C, and D represent different BSL-3Ag animal room designs; these designations are included in the 65% NBAF design phase plans (see Figure 4-2).

Analysis of Option 1: Relative Costs and Other Considerations

The 2012 estimate for NBAF's construction cost is \$1.14 billion, of which \$824 million remains to be funded. In FY 2020, the expected first full year of operations, the facility is estimated to require operation and maintenance (O&M) costs of \$46-\$52 million in operations, management, and security and \$6 million in the salaries of federal DHS staff. The NBAF is expected to include about 350 full-time equivalent staff (DHS, ARS, APHIS, and contractors), including researchers. For O&M and security, DHS estimates a need for 194 contractor staff (142 for O&M and 52 for security) and 36 DHS staff. Hence, the estimated number of full-time equivalent DHS and USDA research staff appears to be about 120. Estimated construction costs per gross ft² of the main laboratory building range from \$203 for general building support space to \$1,197 for BSL-4 space, with an average cost of \$797 per gross ft² for the whole facility. Based on the 65% design estimates, the estimated operational cost is \$90 per gross ft² in 2020 (Johnson and Barrett, 2012).

As a very rough comparison, the recently constructed DHS National Biodefense Analysis and Countermeasures Center was estimated to cost \$143 million to construct (Mary Goobic, DHS, personal communication, May 7, 2012), a facility with approximately 160,000 gross ft² (10,500 net ft² BSL-4, 34,000 net ft² BSL-3, and 11,000 net ft² BSL-2 laboratory space) (www.bnbi.org/faq.html). The Biosecurity Research Institute (BRI) at Kansas State University is a new facility with approximately 113,000 gross ft² facility and has BSL-3 and BSL-3Ag capabilities. The BRI had an estimated construction cost of \$54M (www.bri.k-state.edu). The Friedrich-Loeffler-Institut in Germany also recently completed construction on their high-biocontainment facility which contains BSL-3Ag and ABSL-4 large-animal capacity and approximately 841,000 gross ft² and 237,000 net ft² (Mettenleiter, 2012). The estimated cost for constructing the new facility is €300 million, or about US \$375 million at recent exchange rates for 2012 (Mettenleiter, 2012). However, such figures are difficult to compare directly, and the committee notes that a portion of the increased construction costs for the NBAF derives from facility hardening and the results of site-specific risk assessments. According to DHS, “the NBAF cost per ft² data includes additional costs to meet the recommendations provided in the site-specific risk assessment. These site-specific cost factors should be noted when comparing NBAF cost data to similar facilities” (DHS, 2012b). In contrast, costs for some aspects of the facilities and security at the proposed NBAF could be lower than those currently associated with PIADC; for example, there would be no need for boat transportation to the remote location and no need for secure landing docks in New York, Connecticut, and Plum Island. It was explicitly beyond the committee’s charge to consider site locations of the proposed NBAF; the committee notes these issues only to the extent that they are related to its task to examine the relative costs of the three options that it was asked to discuss.

Although the committee was not given detailed construction cost breakdowns for the proposed NBAF, the overall costs of construction appear to be much greater than costs of comparable recent construction of other biocontainment facilities, including those requiring BSL-4 containment space. For example, the Galveston National Laboratory (GNL, completed in 2008) at the University of Texas Medical Branch in Galveston was specifically hardened to withstand hurricane-force conditions. The two facilities clearly differ in size and missions, but the difference in construction costs (about \$175 million for the GNL) seems high. The substantial proposed costs of the NBAF were explained in part by the need to harden the facility to protect against tornadoes. Consideration of the pros and cons of these costs is beyond the scope of this study; however, it is apparent that further consideration of the potential risks and benefits associated with extensive hardening of the proposed facility may be warranted as requirements and alternatives are considered.

Before turning to a summary of the pros and cons of the NBAF as designed, the committee again notes that it was explicitly outside its scope to consider the location of the proposed NBAF in its discussions and conclusions.

Advantages and Liabilities of Option 1: The National Bio- and Agro-Defense Facility as Currently Designed

The currently designed NBAF has both advantages and liabilities. These are briefly discussed here and summarized in the two lists below.

Because it was designed with the ideal system in mind, the proposed NBAF consolidates all components in a single location and has been designed to meet the current missions of DHS, ARS, and APHIS and proposed mission expansions by these agencies. For example, ARS expects to expand its research beyond foot-and-mouth disease, CSF, and ASF to other zoonotic and emerging pathogens, including vector-borne diseases. APHIS expects to provide enhanced diagnostic services and reference materials for emerging and zoonotic diseases and relevant training. DHS expects to expand its research programs on the development of new foot-and-mouth disease vaccines and of new countermeasures for other high-priority FADs and zoonotic diseases.

BSL-3Ag and ABSL-4 facilities for large-animal research are extremely limited. Most facilities that have high-biocontainment laboratory infrastructure are capable of handling small animals, and some can handle nonhuman primates and possibly medium-size animals (such as sheep and pigs) but not large livestock species (such as cattle and horses). The proposed NBAF provides for such BSL3-Ag and ABSL-4 capacity, which is part of the infrastructure needed to achieve an integrated system to address FAD and zoonotic disease threats. In providing that capacity in the United States, the proposed NBAF does not require the United States to leverage large-animal laboratory capacity through international partners whose priorities and needs may well take precedence over US priorities in the event of an outbreak that requires ABSL-4 containment. Such an outbreak is likely to attract worldwide attention and to impose immediate demands on existing facilities. Finally, by including the components of the ideal system and a variety of biocontainment levels and types of laboratory infrastructure in a consolidated facility, the proposed NBAF avoids the need to move specimens or materials derived from specimens, some or all of which will be select agents, to other facilities. Such specimens may be from experimentally infected animals, suspect FAD samples, forensic samples, or samples from animals infected with unknown agents. Those overall advantages and liabilities are summarized in the lists of bulleted items below.

Advantages

- Includes all laboratory components of the ideal system (as identified in Figure 4-1 and Table 4-1) in a single location.

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- Meets current and expected future mission needs of DHS, ARS, and APHIS.
- Creates needed BSL-3Ag and ABSL-4 large-animal space.
- Provides the United States with in-country infrastructure to address FAD and zoonotic disease threats.
- Avoids need for movement of specimens or materials derived from specimens to other facilities.
- Avoids need to rely on partner entities in the United States or other countries.
- Could function as part of an integrated national strategy that also includes distributed and collaborative partnerships.

Liabilities

- Has substantial costs associated with construction.
- Has substantial costs associated with continued operation and maintenance.
- Has substantial costs associated with expanded program development.
- Has potential for duplication of resources that could be reduced by exploring partnerships.
- Does not fully leverage existing complementary investments.

An additional consideration discussed by the committee is the extent to which priorities and available technologies may change in the approximate decade until an NBAF facility could be constructed and commissioned. A fundamental question is what the workload and associated high-biocontainment space needs will be 10 or more years from now and what technology will be available to achieve research goals. If live large-animal trials for foot-and-mouth disease vaccine development are not being done, space needs may be quite different and possibly much less than the current facility design. As next-generation genetic-sequencing task times and costs decline and there are growing databases of reference genomes, the use of nucleic acid-based detection and diagnostic tests will continue to expand. In most procedures, the requirement for extracting nucleic acid itself will inactivate the agent under study. As a result, the laboratory capacity for agent replication *in vitro* may be less than what is currently needed for detecting and identifying a pathogen. The committee recognizes that current regulations require isolation of an agent for confirmatory diagnosis and that maintaining some capacity and capability for isolation of replicating agents is necessary.

ANALYSIS OF OPTION 2: A NATIONAL BIO- AND AGRO-DEFENSE FACILITY OF REDUCED SIZE AND SCOPE

Envisioning a National Bio- and Agro-Defense Facility of Reduced Size and Scope

The committee emphasizes that laboratory infrastructure at BSL-2, BSL-3E, BSL-3Ag, BSL-4, and ABSL-4 levels includes critical core components that must remain as part of an integrated system and that are currently a part of the proposed NBAF. However, in looking at Option 2 in the statement of task, the committee considered whether an NBAF of reduced size and scope could be designed that would address the critical gaps identified in Chapter 3 while continuing to provide the United States with a comprehensive system to address FAD and zoonotic disease threats. Tables 3-1 and 3-2 list many of the US and international laboratories that have BSL-3Ag and BSL-4 capacity, which may provide opportunities for partnerships to supplement NBAF capacity. Relevant collaborations could include

- In vitro diagnostic work conducted in National Animal Health Laboratory Network (NAHLN) laboratories, in the National Veterinary Services Laboratories (NVSL), and in other federal laboratories, at BSL-2, BSL-3, and BSL-3E containment.
- FAD work (in vitro and in vivo) at the National Centers for Animal Health-NVSL, the Southeast Poultry Research Laboratory (SEPR), state laboratories (such as the BRI), and some university facilities.
- Special-pathogens in vitro work in other federal and academic BSL-4 laboratories.
- In vitro vaccine development work at universities with challenge work as required at federal laboratories, including NBAF for at least FMDv.
- Training at the NBAF on FMDv with some capability for animal demonstration teaching modules at NVSL in Ames, Iowa or at the BRI facility in Manhattan, Kansas. With the exception of FMDv, the BRI facility has appropriate biocontainment for animal inoculation demonstrations.
- Foot-and-mouth disease work—planned only at the NBAF as the sole site in the United States that may be approved to work with FMDv.

The committee identified several components of the NBAF as designed that potentially could be reduced or eliminated if such partnerships were used to meet the needs of an ideal system. They are outlined in red in Figure 4-2 as only one example of what could be considered. Although the committee provides this example of a design modification that could be made for scaling down the facility while still providing critical capabilities for research and diagnostics, a detailed analysis of design specifications and costs was beyond the committee's task and would need to be undertaken by the Department of Homeland Security (DHS) and the NBAF Design Partnership.

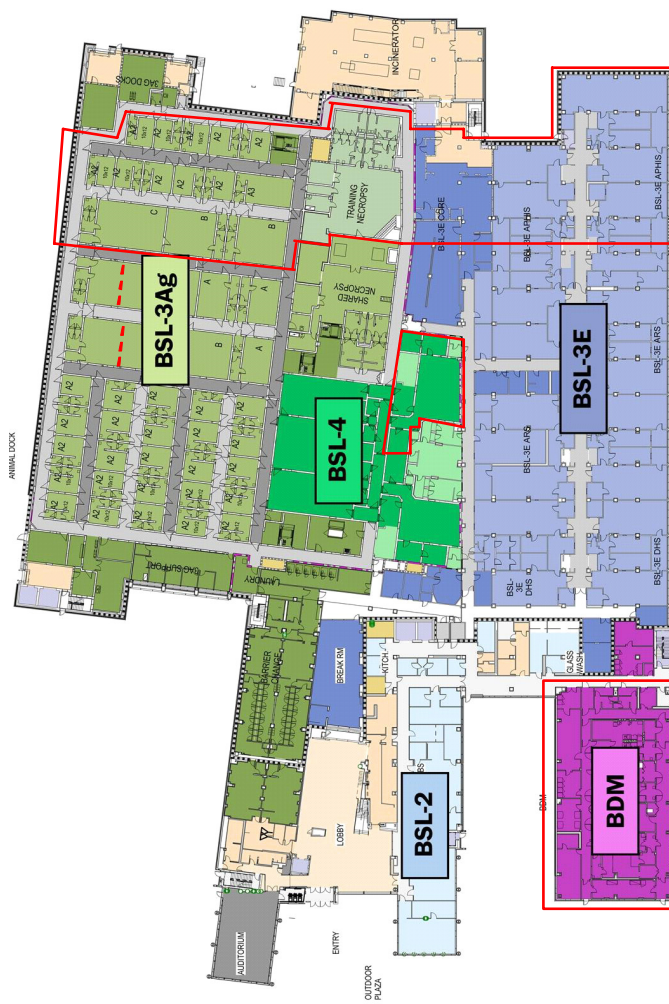


FIGURE 4-2 Re-envisioned NBAF of reduced size and scope, focusing on critical core components for which capacity cannot be effectively provided at other locations. NBAF design plans provided to committee are at 65% phase completion. Areas outlined in red are those that the committee suggests could be eliminated or reduced in scope. SOURCE: Adapted from Johnson and Barrett, 2012.

Examples of the areas that the committee suggests could be considered for reduction or elimination from the proposed NBAF are the Biotechnology Development Module (BDM) and the BSL-3Ag rooms designated for training along with the associated training necropsy room. Other areas that could be considered for reduction are the BSL-3Ag animal rooms, the ABSL-4 small-animal rooms, and the associated BSL-3E and BSL-4 laboratory space.

Both the pilot vaccine production work conducted in the BDM, which is outside the biocontainment envelope, and most teaching and training activities could be conducted in collaboration with facilities in other US federal laboratories, state laboratories, universities, and the private sector. This would include options for hands-on training as well as other approaches, although US-based hands-on training on foot-and-mouth disease would of necessity be limited to the one facility designated by the Secretary of Agriculture for working with FMDv. Table 4-1 identifies some of the types of facilities that could accommodate components of the current NBAF design, and Box 3-2 discusses approaches to training the veterinary workforce in FADs.

BSL-2 laboratory support space is required for *in vitro* research and development, including diagnostics. Although the NAHLN provides important diagnostic capacity to the country, an effective system to address FAD and zoonotic disease threats will nevertheless require that a central facility, such as the NBAF, support the network through confirmatory and reference diagnostics, reference reagent production, proficiency testing, and assay development. Relative to the size and scope of the facility, there does not appear to be an excess of BSL-2 capacity. As a result, the committee concludes that BSL-2 space should not be reduced.

BSL-3E space is similarly required. The committee noted that laboratories in the current design are designated by individual agency (DHS, ARS, and APHIS). It might be possible to reduce space needs by designating use of BSL-3E space by function or common equipment needs or by particular agent being studied, rather than by agency, to avoid duplication.

The proposed elimination of the NBAF teaching and training rooms reduces the proposed space at BSL-3Ag. However, the committee suggests that further modifications of and reductions in BSL-3Ag space might be possible, eliminating one additional corridor (containing one room of type C and two rooms of type B, as shown in Figure 4-2). The block of large-animal rooms (room types B, C, and D) is designed primarily to enable large numbers of agricultural animals to be housed together for animal inoculation experiments and vaccine efficacy trials. Although it is not ideal, the committee suggests that it might be possible to conduct such trials by using a smaller number of animals simultaneously per trial, conducting sequential trials, or connecting adjacent rooms (such as rooms of type B) to form a larger space. The committee also notes that regulations for the emergency licensing of vaccines provide flexibility in conducting postvaccination animal-challenge studies, which can reduce the number of animals per trial and thus the size of isolation rooms needed for trials. It could be argued that between flexibility in the regulations on efficacy studies of new

emergency-use animal vaccines and advances in the development of in vitro methods for evaluating vaccine efficacy, the current NBAF building design, although ideal for large-animal vaccine trials, could be modified to make use of smaller animal rooms. The use of challenge-study protocols with fewer animals at a given time could reduce the construction and maintenance costs of BSL-3Ag animal isolation rooms, reduce the potential for human injuries in dealing with large numbers of animals in confinement, and reduce the total virus load shed at once by the challenged animals. Vaccine challenge studies are discussed more thoroughly in Box 4-1. The flexibility of the rooms could be increased by increasing the number of type B rooms that could be connected as needed and reducing or eliminating rooms of types C and D, indicated by the dashed red lines in Figure 4-2. That option also takes into consideration the changing nature of disease priorities and the potential for advances in science and technology. For example, by the time the NBAF is completed and commissioned in 10 years, the focus on conducting multiple vaccine efficacy trials for foot-and-mouth disease may be reduced because many new vaccines may have already been developed. However, the committee also recognizes that it is important to maintain flexibility in case new high-priority pathogens emerge and new vaccine development efforts are required.

Finally, the committee suggests that some additional facility reductions may be possible through reductions in size and scope of the BSL-3E Special Procedures section and one of the BSL-4 support laboratories. According to DHS, the BSL-3E Special Procedures area is core space that would be used for activities that generate aerosols. It is a large space whose function is not entirely clear to the committee, and it seems feasible to reduce its scope and size. Given the availability of BSL-4 space in numerous facilities in the United States that have space for conducting small-animal trials at ABSL-4, one of the ABSL-4 small-animal suites and associated laboratory space could be considered for elimination.

The committee noted several minor building design aspects that might also be altered or reduced in size and scope to produce cost savings. They included the possibility of reducing the angle of separation between the Auditorium wing and BSL-2 laboratory and office space, making the lobby smaller, and reducing the scale of the building landscaping. However, those types of design components are not central to the committee's charge to evaluate options for providing the needed laboratory infrastructure for a US system to protect against FAD and zoonotic disease threats, so it did not consider them further.

With the reductions in biocontainment space outlined above (elimination of the BSL-3Ag training and necropsy rooms, reduction in and modification of the large BSL-3Ag animal rooms, and consolidation of BSL-3E laboratory space), a figurative "slice" could be removed from the right side of the NBAF biocontainment zone. Along with elimination of the BDM on the left side of the building, this might simplify the redesign of the facility. The committee did not receive information that would enable it to consider the effects of such modifications on the engineering components or the final cost of the facility.

BOX 4-1
Vaccine Challenge Studies

The Virus-Serum-Toxin Act (VSTA; PL 430 of 1913, as amended; 21 USC 151-158) is implemented through regulations codified under CFR 9, Chapter I, Subchapter E, Parts 101-127, enforced by the Center for Veterinary Biologics (CVB), which is a part of APHIS Veterinary Services. The principal aim of the VSTA is to ensure that biological products⁵ are “pure, safe, potent, and efficacious, and not to be worthless, contaminated, dangerous, or harmful” (9 CFR§101.5).⁶ Standards for the determination of purity, safety, potency, and efficacy have been developed through the years on the basis of cooperative research undertaken by USDA-APHIS-VS-CVB and commercial manufacturers. Many potency and efficacy standards have been developed in the private sector (at times under patent protection) with the approval of CVB.

One of the key elements in determining efficacy of a given vaccine is the establishment of statistical significance of a postvaccination response and protection in the animal as claimed by the manufacturer. For example, if a vaccine is claimed to protect pregnant animals from abortion, the claim needs to be statistically proven either with challenge studies in vaccinated pregnant animals or with controlled field experiments that use vaccinated and nonvaccinated animals exposed naturally by a statistically similar pathogenic challenge. Perhaps one of the most common ways of establishing the efficacy of a vaccine is to perform experiments that include two groups: nonvaccinated animals challenged with the pathogenic agent (control group) and vaccinated animals challenged with the pathogenic agent (vaccinated group). The preferred experimental setup is to have the control and vaccinated animals housed together and to challenge all at the same time with the same infection protocol.

To gain sufficient statistical significance for a challenge study, it is desirable that an experiment be done with as many animals as is practical. In the case of foot-and-mouth disease vaccine challenge studies, the World Organisation for Animal Health (OIE) recommends the use of the percentage of protection against generalized foot infection (PGP) test. In this test, 16 foot-and-mouth disease-seronegative cattle at least 6 months old “are vaccinated with a bovine dose by the route and in the volume

(Continued)

⁵The term *biological products* is defined as including “vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants, certain cytokines, antigenic or immunizing components of live organisms, and diagnostic components, that are of natural or synthetic origin, or that are derived from synthesizing or altering various substances or components of substances as microorganisms, genes or genetic sequences, carbohydrates, proteins, allergens, or antibodies” (9 CFR§101.2).

⁶Definitions: *purity*, “quality...free of extraneous micro-organisms and extraneous material (organic or inorganic)”; *safety*, “freedom from properties causing undue local or systemic reactions”; *potency*, “relative strength...as determined by test methods”; *efficacy*, “specific ability or capacity... to effect the result for which it is offered when used under the conditions recommended by the manufacturer” (9 CFR§101.5).

BOX 4-1 Continued

recommended by the manufacturer. These animals and a control group of two non-vaccinated animals are challenged 4 weeks or more after vaccination...by inoculating a total of 10,000 BID₅₀ [bovine infectious doses of the challenge strain] intradermally into at least two sites on the upper surface of the tongue. Unprotected animals show lesions at sites other than the tongue within 7 days after inoculation. Control animals must develop lesions on at least three feet; for routine prophylactic use, the vaccine should protect at least 12 animals out of 16 vaccinated” (OIE, 2008).

For statistical and quality-assurance purposes, the ideal is that all challenged and control animals be housed together in the same room and that the challenge be done simultaneously to all animals with the same preparation. That is the reason for the desire to have biocontainment BSL-3Ag facilities to house at least 18 large animals in the same room for challenge studies for foot-and-mouth disease vaccines, as has been the case for the additional isolation rooms being commissioned at PIADC and included in the design of NBAF (rooms of types C and D).

The VSTA includes provisions for exemptions under 9 CFR§106.1:

“The Administrator may exempt any biological product from one or more of the requirements of this subchapter if he determines that such product will be used by the Department or under the supervision or control of the Department in the prevention, control or eradication of animal diseases in connection with (a) an official USDA program; or (b) an emergency animal disease situation, or (c) a USDA experimental use of the product.”

Given that vaccines against FAD agents (such as FMDv) will have to be used under emergency declaration by the Secretary of Agriculture under authorities provided by the Animal Health Protection Act (7 USC, Chapter 106), there should be adequate flexibility in applying the above VSTA exemption provisions to establish efficacy data for foot-and-mouth disease vaccines and other vaccines intended solely for emergency use in the United States. For example, efficacy testing for foot-and-mouth disease vaccine candidates could be done using the PPG test protocol recommended by the OIE and doing challenge studies in groups of nine animals at a time (one control and eight vaccinates) simultaneously or sequentially (using NBAF rooms of type B) to achieve data on the required number of 16 vaccinated-and-challenged and 2 control-and-challenged animals. Two or three smaller adjacent isolation rooms could also be connected with opening partitions so that for a given challenge case, all animals could technically be considered “within the same confined space”, as has been the case at PIADC. Closing the partitions (gasketed doors) would allow the use of individual rooms.

Smaller-scale animal vaccine challenge studies are also needed for the determination of potency of new vaccines. In such cases, groups of four or five animals are vaccinated with full doses and fractions of full doses (one-half, one-fourth, one-tenth, and so on) to establish the optimal concentration of antigens that elicit a protective immune response. Once potency is established, the final large-scale efficacy challenge studies are conducted.

Shelling Non-Critical Components of the Currently Designed NBAF

The committee also discussed the possibility of “shelling”, or partially constructing the NBAF as designed. That might enable near-term cost savings by focusing construction on the sections of the facility that encompass the critical core functions identified by the committee and allowing later completion of other building components if future budgets and priorities allow. That possibility might realize some cost savings in the short term, but the committee concluded that it is implicitly a subset of Option 1, the currently designed NBAF, with the only difference being a deferral or partial allocation of necessary funding for construction and operation. While realizing short-term savings, this option would not result in long-term cost savings compared to Option 1. As a result, the committee did not consider this possibility in further detail, although it raises the possibility as an additional alternative that could be considered by DHS to reduce near-term costs.

Analysis of Option 2: Laboratory Capacity

In an NBAF of reduced size and scope described by the committee, all biocontainment levels are retained; as a result, this option does not decrease capability but rather proposes some decreases in capacity within a central laboratory. A streamlined NBAF must function as part of an overall system that maintains the critical core competencies needed to address US FAD and zoonotic disease threats. In order to accomplish this goal, a streamlined NBAF would require the formation of collaborations with existing federal, university, and private sector laboratories to supplement its capacity. As indicated in Table 4-1 and discussed above, a variety of possible options exist for meeting some of these infrastructure needs. The specific arrangements of which types of supplemental capacity would be available at which potential partner institutions and the practical details of how such a system would function effectively would need to be established by DHS, USDA, and other relevant federal and non-federal partners. Taking the redesign steps shown in Figure 4-2 would reduce the size of the proposed facility (see Table 4-4). The committee notes that drawing on partnerships to reduce some of the potential redundancies in US laboratory capacity for addressing FADs and zoonotic diseases raises a theoretical possibility that system capacity could be overloaded or insufficient in the event of simultaneous disease outbreaks. As a result, the US could consider maintaining memoranda of understanding with foreign and domestic laboratories in case of an emergency.

TABLE 4-4 Approximate Facility Size and Construction Cost Reductions

	Estimated Net Square Footage Reduction ^a	Estimated Gross Square Footage Reduction ^b	Cost per Gross Square Foot (\$) ^c	Estimated Construction Cost Savings (\$) ^d
BDM	8,320	20,800	758	15,774,000
BSL-3Ag	13,481 (estimated reduction of 25% space)	53,925	977	52,685,000
BSL-3E (including Special Procedures laboratory)	9,365 (estimated reduction of 25% space)	37,360	878	32,802,000
BSL-4	2010 (estimated reduction of 15% space)	8040	1,197	9,624,000
Total				110,885,000

^aNet square footage reductions were estimated in various types of laboratory space on the basis of the NBAF 65% design plan presented by DHS (Johnson and Barrett, 2012) and additional net and gross square footage laboratory information provided to the committee (DHS, 2012b); see also Table 4-5.

^bThe difference between the net square footage and gross square footage values of the BSL-3Ag, BSL-3E, and BSL-4 laboratory components provided by DHS to the committee is 4, a multiplication factor that presumably accounts for infrastructure floors above and below laboratory floors and other supporting infrastructure requirements.

^cSource: DHS, 2012b.

^dThese figures should be considered general estimates only, on the basis of information given by DHS to the committee about the NBAF 65% design plans (DHS, 2012b; Johnson and Barrett, 2012). The committee cannot predict exact net and gross square footage reductions associated with its proposal and is unable to account for additional costs related to facility redesign and timeline adjustments or for potential cost savings from future reductions in operations costs.

Analysis of Option 2: Relative Costs and Other Considerations

The streamlined NBAF described above envisions a scaled-back building design. Although the committee has attempted to keep as many elements of the current building intact as feasible, pursuing this option would require at least some building redesign. On the basis of gross square footage construction cost estimates provided by DHS, an approximately 25% reduction in size of the NBAF as shown in Figure 4-2 and provided as one example could result in a construction cost savings of approximately \$110 million (Table 4-4). This estimate is provided as a relative cost reduction only, and does not take into account the cost of redesign and delays in construction that might increase the cost as well as the additional expenses needed to continue operations of the Plum Island facility in the interim. DHS has noted that a facility redesign would need to return to the 15% design stage to re-evaluate the complex mechanical, electrical, plumbing, and other engineering systems associated with biocontainment laboratories and that changes in the size and scope of the main laboratory building

depicted in Figure 4-2 might affect support facilities and require additional changes (DHS, 2012b). The committee recognizes that a redesign process would add construction time and costs that could offset at least some of the potential cost savings from reducing the size and scope of facility components.

In its presentation to the committee, DHS estimated that a facility redesign would cost \$50-60 million and add 12-18 months to the process. DHS later refined those estimates, using an example in which the BSL-4 component was eliminated from the main laboratory and estimating a 30-month delay due to redesign and contract procurement. At 4% annual cost increases, the result would be an overall cost increase of \$177 million. The committee found that it did not have enough information to analyze that estimate objectively, but it notes that an NBAF with a smaller footprint and reductions in high-biocontainment laboratory space might have lower sustained operations costs. Other long-term cost savings may be realized by making more efficient use of the existing networks of US laboratory capacity, particularly for *in vitro* and small animal studies and work with zoonotic pathogens. However, additional costs of using partnerships to meet US needs for countering disease threats include the costs associated with creating and maintaining the contractual arrangements and contract management necessary to partner with other facilities for work that would not be performed at the currently planned NBAF. Overall costs across the total federal budget would be influenced by the extent to which activities were shifted to existing federal laboratory facilities that currently have additional or under-used capacity and to non-federal facilities; total cost implications are thus unknown given the information and rough estimates provided to the committee. Analyzing the actual costs of building an NBAF of reduced size and scope was beyond the scope of what the committee could address given the extremely tight schedule for the study and the limited information available. This would need to be explored further to gain a detailed understanding and estimate.

Advantages and Liabilities of Option 2: A National Bio- and Agro-Defense Facility of Reduced Size and Scope

The concept of an NBAF of reduced size and scope from the current design has both advantages and liabilities. Because it would continue to incorporate laboratory infrastructure at BSL-3Ag, BSL-4, and ABSL-4, it would continue to address the critical core needs of an ideal system for dealing with FAD and zoonotic disease threats identified by the committee. It would also still allow the consolidation of mission needs of DHS, ARS, and APHIS in a single location and meet the overall needs of countering disease threats to the nation. This option also makes more efficient use of the network of recently expanded US high-containment laboratory capacity and avoids some duplications of laboratory infrastructure. In addition, an NBAF of reduced size and scope, in conjunction with an integrated network of laboratories, would foster greater collaboration

between researchers and greater understanding of missions as part of the overall integrated system for countering disease threats. Finally, by relying on a network of partners, this option may provide increased flexibility to re-evaluate laboratory infrastructure needs periodically in light of new and emerging disease priorities and technologies.

In contrast, reducing the NBAF in size and scope means that some components of the ideal system for countering FAD and zoonotic disease threats (such as teaching and training and vaccine production) are not housed in a single facility and would need to be obtained in collaboration with a network of other facilities. Such a system may require the movement of specimens or materials derived from specimens, some of which will be select agents, to other facilities. It would also require effective coordination among the agencies involved. Current policies and regulations, such as facility requirements for select-agent authorization, would need to be examined and perhaps modified. The option would also require interagency cooperation in developing agreements regarding the use of laboratory space and entail a need to explore and create agreements with partner facilities. In addition, because of reductions or consolidations in space, this option might require DHS and USDA to set priorities because they may not be able to expand their research programs as quickly or as widely as they have proposed and would probably need to adjust planned numbers and timelines for large-animal vaccine efficacy studies.

The ultimate cost implications of Option 2 compared to Option 1 are unclear based on the limited information provided to the committee and would need to be studied in greater detail.

The overall advantages and liabilities considered by the committee are summarized in the lists of bulleted items below.

Advantages

- Provides an approximately 25% smaller NBAF that may have reduced construction costs (although the actual cost implications are not clear).
- May provide lower sustained costs of NBAF operation; may also provide some longer-term cost savings by making more efficient use of existing US laboratory infrastructure and partnerships.
 - Addresses critical core needs for BSL-3Ag, BSL-4, and ABSL-4.
 - Still allows DHS, ARS, and APHIS mission consolidation in a single location.
 - Meets overall needs of countering disease threats to the nation.
 - Provides in-country capacity.
 - Makes more efficient use of recently expanded US laboratory capacity.
 - Fosters greater collaboration and understanding between researchers as part of the integrated US system for countering FAD and zoonotic disease threats.

- Changes the approach to addressing animal diseases by drawing on scientific and research expertise in other federal and non-federal laboratories, providing both intellectual benefits and possible cost savings through increased efficiencies by avoiding duplication or relocation of scientists at the NBAF and fostering collaboration.
- Provides more flexibility for periodically re-evaluating infrastructure needs in light of new and emerging disease priorities and technologies.

Liabilities

- Not all components of the ideal system are housed in a single integrated facility.
- May require movement of specimens or materials to other facilities.
- Requires interagency cooperation in developing agreements in the use of laboratory space.
- Requires creation of agreements with partner facilities.
- Requires funding commitments to partner facilities for collaborative work and establishment of grant-management capacity to oversee collaborations.
- Would have policy implications that would need to be explored further.
- Might require DHS and USDA to make priority-setting decisions.

ANALYSIS OF OPTION 3: MAINTAINING CURRENT CAPABILITIES AT PLUM ISLAND ANIMAL DISEASE CENTER WHILE LEVERAGING ABSL-4 LARGE-ANIMAL CAPACITY THROUGH FOREIGN LABORATORIES

The third option in the statement of task to be considered by the committee was to maintain the current capacity of PIADC and to use BSL-4 and ABSL-4 large-animal facilities that are currently available at foreign laboratories. PIADC does not contain infrastructure for conducting research at BSL-4 and ABSL-4. The committee was informed by DHS that BSL-4/ABSL-4 laboratory facilities could not be constructed at PIADC; the committee therefore did not further consider the possibility of building BSL-4/ABSL-4 space at PIADC.

Current Situation of Plum Island Animal Disease Center Capacity and Capabilities

PIADC has a long history of serving the nation as the sole high-biocontainment laboratory for performing research and diagnostic investigations on foot-and-mouth disease and other FADs. A historical perspective of the role of PIADC in FAD work is presented in Appendix C. PIADC remains the only

laboratory in the United States that has the capability and capacity to address the threat of foot-and-mouth disease. The committee notes that foot-and-mouth disease is appropriately still considered the highest-priority disease threat to US agriculture because of its highly contagious nature, as demonstrated by the continued occurrence of foot-and-mouth disease outbreaks in many areas of the world (such as South Korea), the movement of hundreds of people and countless goods to the United States daily, the continuous movement of FMDv strains around the world (such as the appearance of SAT-2 in areas of north Africa)⁷, and the threat of bioterrorism with FMDv as a means of disrupting the economic and social infrastructure of the United States. It is imperative that the nation maintain an infrastructure to address countermeasures against a FMDv outbreak, whether naturally occurring or intentional.

With regard to the core laboratory needs identified above and used as a framework for considering Options 1 and 2, PIADC currently provides capability and capacity for

- In vitro diagnosis—maintains full range of diagnostics for confirmatory diagnosis of index cases of foot-and-mouth disease, CSF, ASF, and other FADs (it should be noted that confirmatory testing for a number of other FADs is also performed at NVSL, Ames); presumptive-level testing in outbreak investigations other than priority 1 is now allowed and performed in NAHLN laboratories;⁸ some BSL-2 work is done at NVSL, Ames and at PIADC, including preparation of reference reagents and proficiency-testing support.
 - FAD work (in vitro and in vivo); it should be noted that work with some pathogens or species is done at NVSL, Ames and SEPRL.
 - Special-pathogens work, but no capacity for BSL-4/ABSL-4.
 - Vaccine development—some in vitro and selected challenge work; two new challenge-study rooms are being commissioned and will increase capacity.
 - Foot-and-mouth disease work—all done at PIADC in accordance with current laws.
 - Training—nearly all FAD training with animal demonstrations; some laboratory training is done at CVB in Ames, IA.

The laboratory space currently available at PIADC is summarized and compared to the equivalent biocontainment level space in the proposed NBAF in Table 4-5. The total space available in the main buildings at PIADC is 142,700 net ft² and 245,940 gross ft², compared to 176,000 net ft² and 580,200 gross ft² available in the main building of the proposed NBAF (Johnson and Barrett,

⁷SAT-2 foot-and-mouth disease virus is one of three major virus serotypes designated as South African Territories (SAT) 1-3. SAT-2 is the most common type causing foot-and-mouth disease in sub-Saharan Africa and West Africa (Bastos et al., 2003).

⁸The procedures for conducting investigations of potential foreign animal diseases are outlined in Veterinary Services Memorandum 580.4 (USDA, 2010).

2012). The committee notes that the condition and functionality of the space are also important considerations beyond a direct comparison of square footage.

TABLE 4-5 Comparison of Space Available at PIADC and the Proposed NBAF

	Space available at PIADC (net square feet)	Space available at proposed NBAF (net square feet)
BSL-4 laboratories	0	13,400
BSL-3Ag and BSL-3E laboratories	72,400	81,100 ^a
BSL-2 laboratories	5,300	9,700
BSL-2 Biotechnology Development Module	0	8,300
Office and support space	65,000	63,500

SOURCE: Johnson and Barrett, 2012.

^aThe proposed NBAF includes 37,460 net ft² of BSL-3E and 53,925 net ft² of BSL-3Ag laboratory space (including animal support), which totals 91,385 net ft² (DHS, 2012b). The approximately 10,285 net ft² difference between this total and the 81,100 net ft² listed above presumably represents the animal support component.

Land, buildings, and other facilities of PIADC were transferred to DHS in June 2003. Since then, the DHS Science and Technology Directorate has been responsible for operating and maintaining the Plum Island site. Operational services—including security, building and site maintenance, and operation of marine vessels and transportation—are contracted out to an independent private organization. DHS provides the director of PIADC. ARS and APHIS have established agreements with DHS for their continued operations at PIADC, and each provides a director for its research and diagnostic programs. Each USDA agency is responsible for providing its own scientific and technical support staff and for paying for its own scientific operations (cost of diagnostic operations or cost of bench and animal research activities).

Analysis of Option 3: Laboratory Capacity

PIADC has been able to provide the basic facilities for research, diagnosis, and training needed for the protection of the United States against FADs for more than 50 years, but there are several important limitations in its laboratory capacity. Some remodeling of the main biocontainment building, Building 101 (now approaching 60 years old), was done in 1994, and the building of two new animal holding rooms and the remodeling of one necropsy room have provided needed additional space for current work. However, the basic building structure, the size of the animal rooms, and other ancillary infrastructures are seriously deficient for state-of-the-art research and diagnostic work at high biocontain-

ment. The building does not meet current standards for BSL-3Ag and does not have capabilities for BSL-4 and ABSL-4. All physical support for the building—such as high-efficiency particulate air filters, heating, ventilation, and air-conditioning—is within the biocontainment envelope, where maintenance and repairs are more difficult, expensive, and time-consuming. PIADC requires continuing high annual operating costs and will continue to need renovations. Finally, as noted above, the committee was advised that adding BSL-4/ABSL-4 containment to PIADC was not possible, given the need for political and local acceptance to conduct such work on Plum Island. If this is correct, the building cannot meet all the components of an ideal system as identified by the committee. The need for replacement facilities and the decommissioning of existing buildings were noted in the previous studies of the facility and in the recent 2006 DHS decision to build the NBAF on the US mainland (NRC, 1983; USDA, 1994, 1999; DHS, 2008b; 74 Federal Register, 2009).

Pursuing Option 3 would therefore require the United States to seek ABSL-4 large-animal laboratory capacity through partners such as foreign laboratories. BSL-4 capabilities for in vitro and small-animal work exist at current facilities in the United States and abroad.⁹ The United States lacks ABSL-4 large-animal capacity, and such capacity is extremely limited in the entire Western Hemisphere (only the facility in Winnipeg, Canada has the capacity for ABSL-4 work in livestock, and this facility is small). Option 3 would require the United States to obtain this capacity, when it is needed, through partnerships with foreign laboratories; Table 3-2 identifies some of the international facilities that have ABSL-4 capabilities.

Despite the limitations noted above, the committee emphasizes here and elsewhere in this report that the facilities available at PIADC must be maintained until a new US biocontainment facility is constructed and commissioned. The committee also believes that, given the current lack of US ABSL-4 facilities that could handle large animals, it is advisable for the United States to enter into formal cooperative agreements now with foreign laboratories to conduct research that may require ABSL-4 large-animal containment. Such agreements could be established in the interim until a new US biocontainment facility with ABSL-4 large-animal space is built and commissioned. As indicated in the history of PIADC (Appendix C), successful international research cooperative agreements existed before the creation of PIADC to work with FMDv in several European laboratories, and this model could be replicated for the emergency use of ABSL-4 facilities until this critical capacity is available in the United States or as an emergency supplement to future US ABSL-4 large-animal capacity.

⁹As indicated above, the committee does not agree with USDA and DHS statements that BSL-4 capabilities are required for unpacking diagnostic samples or for basic diagnostic procedures when nucleic acid detection technologies are used. Such work can be and is performed safely in regular BSL-3 or BSL-3E facilities.

Relative Costs

Annual PIADC operating costs in FY 2020 are estimated at \$56 million (\$50 million for operations and maintenance, \$6 million for DHS salaries). That does not include the salaries and operations of ARS and APHIS personnel and programs at PIADC. However, the aging PIADC facilities are in need of substantial improvements. Initial rough estimates total \$90 million for short-term improvements (including improvements in the liquid-waste decontamination facility, Plum Island and Orient Point Harbors, information technology upgrades, utility and building upgrades, security hardening, detection and access control, and marine-vessel replacement and lighthouse restoration), while long-term improvements are estimated at \$210 million if PIADC is required to maintain its existing mission and to continue operating for another 25 years.

Advantages and Liabilities of Option 3: The Plum Island Animal Disease Center

PIADC is currently the only US facility that can provide several of the critical core functions of an integrated system to address FAD and zoonotic disease threats and is the only laboratory in the United States that is authorized to conduct research, diagnostics, and training related to foot-and-mouth disease. It represents an existing investment that would avoid the costs of construction of a new biocontainment facility. If a full commitment were made to improving and maintaining PIADC, the avoidance of constructing a new facility would also obviate the need for a facility transition period with a potential temporary loss of function. In addition, capital improvements and other investments are needed at PIADC over the next 10 years, whether the facility is maintained only until a new facility is constructed or continues to serve as the central laboratory for a US system to address FADs and zoonotic diseases over a longer period. Thus, pursuing Option 3 would continue to realize the benefit of those investments over a longer period. It would also exclude the risk that necessary investments are being forgone to save costs during the years just before PIADC cedes its activities to a new NBAF. By relying on the ABSL-4 capacity of other existing US laboratories (for in vitro and small-animal work) or foreign partners (for ABSL-4 large-animal work), this option also saves the United States from investing in in-country BSL-4/ABSL-4 capacity. Cooperative agreements with foreign partners in case of an ABSL-4 need also enhance international cooperation in FAD and zoonotic disease research.

In contrast, continuing to maintain and operate PIADC even without renovation entails substantial annual costs of about \$60-90 million. The facilities at PIADC are aging and do not meet current standards for high-biocontainment laboratories, including the 2004 Homeland Security Presidential Directive 9 [HSPD-9 (2004)] mandate to build new biocontainment facilities. Under Option

3, the United States would not have a modern biocontainment facility for FAD research, particularly research on foot-and-mouth disease, and would not have ABSL-4 capacity. The need to rely on foreign partners for ABSL-4 large-animal capacity might limit the availability of such capacity in a time of emergency if US needs were considered secondary to the needs and priorities of the partner country. Finally, the long-term maintenance of PIADC will continue to experience difficulties in hiring new high-level scientists to work there; this is a challenge because of the aging infrastructure and the remote location. The committee did not further consider this or other site-specific issues as site was prohibited from consideration in the statement of task.

The overall advantages and liabilities considered by the committee are summarized in the lists of bulleted items below.

Advantages

- Is an existing US facility that provides many of the laboratory infrastructure components needed and would avoid the costs of constructing a new replacement facility.
- Is the only US facility that is authorized to conduct research, diagnostics, and training in foot-and-mouth disease.
- If there were a full commitment to PIADC, a transition period to a new facility with a window of potential loss of function would not be needed.
- Realizes the benefits of the capital renovations and improvements that must be made for a longer period.
- Does not require investment in BSL-4/ABSL-4 capabilities in the United States.
- Could function as part of an integrated national system that also includes distributed and collaborative partnerships
- Enhances international cooperation for work on FADs and emerging animal and zoonotic diseases.

Liabilities

- Has a high cost to maintain and operate PIADC.
- Does not provide the United States with a modern biocontainment facility for FAD and zoonotic disease research, particularly on foot-and-mouth disease.
- Does not provide the United States with BSL-4/ABSL-4 capability for handling large animals.
- Requires establishing agreements with foreign partners for access to BSL-4 laboratories and presumably funding to support the collaborations.

- May limit the availability of BSL-4 capabilities in times of need, depending on priorities of other countries.
- Continues to highly limit ABSL-4 large-animal capacity in the Americas.
- Maintaining PIADC long term will continue to compound the difficulties in hiring new high-level scientists to work there due to the continued isolation of the national laboratory site from academic and other research and development centers.

CONCLUSIONS ABOUT THE THREE OPTIONS

As a result of its evaluation of the three options in its statement of task, the committee finds

- Option 1: The NBAF as currently designed includes all components of the ideal laboratory infrastructure in a single location and has been designed to meet the current and anticipated future mission needs of DHS, ARS, and APHIS; but the proposed facility also has drawbacks (**Conclusion 1**).
- Option 2: A partnership of a central national laboratory of reduced scope and size and a distributed laboratory network can effectively protect the United States from FADs and zoonotic diseases, potentially realize cost savings, reduce redundancies while increasing efficiencies, and enhance the cohesiveness of a national system of biocontainment laboratories. However, given the limited and insufficient information provided by DHS, the cost implications of reducing the scope and capacity of a central facility cannot be known without further information and study (**Conclusion 2**).
- Option 3: Maintaining PIADC and drawing on the ABSL-4 large-animal capacity of other partners would utilize an existing US facility that provides some of the needed laboratory infrastructure components and would avoid the costs of constructing a new replacement facility. However, the facilities at PIADC are aging and do not meet current standards for high-biocontainment laboratories, there are substantial costs associated with maintaining and operating it, it lacks BSL-4 and ABSL-4 large-animal capabilities, and the committee was informed by DHS that such facilities could not be constructed at PIADC (**Conclusion 3**).

OTHER OPTIONS

The committee recognizes that the three options it was asked to address in the statement of task are not the only possible options for meeting the nation's laboratory infrastructure needs with regard to animal and public health. For example, the possibility of constructing BSL-4/ABSL-4 space on Plum Island could be revisited; the option of constructing an entirely new laboratory facility

on Plum Island, perhaps connected to the mainland by a bridge, could be considered; NBAF could be built only as a replacement for the existing facility on Plum Island, with newly constructed ABSL-4 large-animal space co-located with existing ABSL-4 laboratory space now used to study zoonotic diseases in small animals and primates; or a variety of other options. As a result, the committee notes that there are numerous possibilities for creating an integrated national strategy and a network of collaborative partnerships to achieve the ideal system for addressing FAD and zoonotic disease threats. However, evaluating the full array of options and their relative advantages and disadvantages fundamentally draws not only on infrastructure needs but also on discussions of site locations, risk assessments, political considerations, adaptability for the future, and other elements explicitly outside of the committee's statement of task, aspects of which have also been the subject of previous reports.

SUMMARY

In this chapter, the committee has described how an NBAF of reduced size and scope might be envisioned and has discussed the advantages and liabilities of the three options that it was asked to consider in its statement of task. On the basis of the committee's research and discussions, Chapter 5 provides the committee's additional conclusions and recommendation on how the laboratory research needed to enable the United States to address FADs and zoonotic diseases might be effectively assembled.

REFERENCES

- ASTMH (American Society of Tropical Medicine and Hygiene). 2003. The American Committee of Medical Entomology Arthropod Containment Guideline (Version 3.1). *Vector Borne and Zoonotic Diseases* 3(2):57-98.
- Bastos, A.D., D.T. Haydon, O. Sangaré, C.I. Boshoff, J.L. Edrich, and G.R. Thomson. 2003. The implications of virus diversity within the SAT 2 serotype for control of foot-and-mouth disease in sub-Saharan Africa. *Journal of General Virology* 84:1595-1606.
- CDC (Centers for Disease Control and Prevention). 2009. Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Ed. (CDC) 21-1112. US Department of Health and Human Services, Public Health Services, Centers of Disease Control, National Institute of Health [online]. Available: <http://www.cdc.gov/biosafety/publications/bmb15/BMBL.pdf> (accessed June 5, 2012).
- CRS (Congressional Report Service). 2008. The National Bio- and Agro-Defense Facility: Issues for Congress. Updated November 25, 2008. Order Code RL34160.
- Colby, M. 2012. DHS Science Program. Presentation at the Meeting on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, April 13, 2012, Washington, DC.
- DHS (Department of Homeland Security). 2007a. Additional Physical, System, and Management Controls Can Enhance Security at Plum Island (Redacted). OIG-07-43. US Department of Homeland Security, Office of Inspector General.

- DHS. 2007b. Final Selection Memorandum For Site Selection for the Second Round Potential Sites for the National Bio and Agro-Defense Facility (NBAF). July 2007. US Department of Homeland Security, Science and Technology Directorate.
- DHS. 2008a. An Addendum to the Final Selection Memorandum for the Site Selection for the Second Round Potential Sites for the National Bio and Agro-Defense Facility (NBAF), Dated July 2007. Memorandum for the Record. US Department of Homeland Security, Science and Technology Directorate.
- DHS. 2008b. National Bio and Agro-Defense Facility: Final Environmental Impact Statement. December 2008. US Department of Homeland Security, Science and Technology Directorate, Office of National Laboratories.
- DHS. 2012a. NBAF Updated Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment. Final Report, Vol. 1, February 2012 [online]. Available: http://www.dhs.gov/xlibrary/assets/st/nbaf_updated_ssra_volume_i.pdf (accessed May 30, 2012).
- DHS. 2012b. DHS Responses and Supporting Materials to the Questions Sent by the Committee. April 20, 2012.
- Federal Register. 2009. Record of Decision for the National Bio and Agro-Defense Facility Environmental Impact Statement. US Department of Homeland Security, Science and Technology Directorate. Washington, DC: US Government Printing Office. 74(11):3065-3080 [online]. Available: <http://edocket.access.gpo.gov/2009/E9-914.htm> (accessed June 5, 2012).
- Johnson, J., and L. Barrett. 2012. PIADC & NBAF. Presentation at the Meeting on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, April 13, 2012, Washington, DC.
- Kappes, S. 2012. ARS Science Program. Presentation at the Meeting on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, April 13, 2012, Washington, DC.
- Lautner, E. 2012. APHIS Science Program. Presentation at the Meeting on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, April 13, 2012, Washington, DC.
- Mettenleiter, T.C. 2012. Welcome to the Friedrich-Loeffler-Institut Federal Research Institute for Animal Health. Presentation at the Meeting on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities, April 13, 2012, Washington, DC.
- NDP (National Bio- and Agro-Defense Facility Design Partnership). 2011. 50% Construction Documents, Basis of Design, August 19, 2011 (as cited in DHS, 2012a).
- NRC (National Research Council). 1983. Long-Term Planning for Research and Diagnosis to Protect US Agriculture from Foreign Animal Diseases and Ectoparasites. Washington, DC: National Academies Press.
- NRC. 2005. Critical Needs for Research in Veterinary Science. Washington, DC: The National Academies Press.
- OIE (World Organisation for Animal Health). 2008. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (mammals, birds and bees). 6th edition. Version adopted by the World Assembly of Delegates of the OIE in May 2009. Paris: Office International des Epizooties.
- USDA (US Department of Agriculture). 1994. Final Report: Task Force on Biocontainment Facilities for Foreign Animal Disease Research and Diagnostic Activities. Agriculture Research Service (ARS) and Animal and Plant Health Inspection Service (APHIS). March, 1994.

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- USDA. 1999. Report of the Strategic Planning Task Force on USDA Research Facilities: A 10-year Strategic Plan. Report and Recommendations. Washington, DC: US Government Printing Office.
- USDA. 2010. Veterinary Services Memorandum No. 580.4. Procedures for the Investigation of Potential Foreign Animal Disease/Emerging Disease Incidents (FAD/EDI). John R. Clifford, Deputy Administrator, Veterinary Services, August 18, 2010.

5

Overarching Conclusions and Recommendation

Earlier chapters of this report examined the literature on the risk of infectious disease in US livestock production, identified the capabilities necessary to counter disease threats and protect the food supply and public health, and explored the strengths and weaknesses of three scenarios for providing laboratory functions relative to the identified capabilities. This chapter analyzes the options in light of the broader context of the Department of Homeland Security's (DHS's) need for advice on how to assemble the laboratory capacity to protect the food supply and animal agriculture from the threat of infectious disease. In providing this analysis, the committee has taken into consideration the current budget realities of DHS and other federal agencies, factors that drive costs of laboratory construction and operation, assumptions about what is possible and what is acceptable with regard to the three proposed scenarios, and its findings regarding the resources that are available to enhance the nation's current capacity to safeguard animal health, public health, and food security.

As this and previous NRC reports describe, threats to US agriculture from foreign animal diseases (FADs), zoonotic diseases, and emerging diseases are growing, and it is imperative to establish research, diagnostic, and surveillance laboratory capabilities commensurate with the size and value of the US animal agriculture industry to prevent or mitigate a disease outbreak that could have devastating effects on human and animal lives and livelihoods. The committee finds that the country's laboratory infrastructure is lacking in several ways, but especially with regard to modern biosafety level 3 agriculture (BSL-3Ag) and biosafety level 4 (ABSL-4) large-animal containment capabilities, which are among the critical core functions of a national system. The proposed National Bio- and Agro-Defense Facility (NBAF) as currently designed is envisioned as a high-biocontainment laboratory that could serve to provide such capabilities within a national system, but the proposed facility also has drawbacks.

In presenting the agency's study request to the committee on April 13, 2012, DHS Under Secretary O'Toole noted that although DHS remains convinced of the need for the NBAF, the source of funds to construct it has yet to be identified. She pointed to cuts of 53% in DHS's science and technology division budget, the many competing needs in the agency (for both facilities and research), the general fragility of the national economy, and the collapsed real-estate value of the Plum Island property, whose sale was once envisioned as a source of revenue for building the NBAF.

At the same time, DHS Under Secretary O'Toole noted that given the high stakes of the threat of animal disease for the large US agricultural economy, not providing an adequate laboratory infrastructure could also be very costly in the long run. That assessment provided a context for the work of the committee, which set about examining the two proposed alternatives to the NBAF as currently designed.

ANALYSIS OF THE THREE OPTIONS

The Plum Island Animal Disease Center (PIADC) is currently the only US facility that can provide many but not all of the capabilities necessary for a central national laboratory as part of the US system for addressing FAD and zoonotic disease threats. However, it has no capacity for ABSL-4 large-animal work, and its BSL-3Ag space is currently considered substandard. The committee was informed by DHS that adding ABSL-4 capacity to PIADC would not be possible, given the need for political and local acceptance of zoonotic disease work on Plum Island.

Even if continued renovations of such laboratory space at PIADC were contemplated, it might not ultimately increase the utility of the facility. PIADC is aging and increasingly inefficient, and there is a relatively high annual cost associated with continually renovating and maintaining it. That cost could be a drain on the system in the long term, and funds might be better placed in supporting disease surveillance or diagnostic development and research. Inasmuch as PIADC is the only facility permitted to work on foot-and-mouth disease virus (FMDv), the committee finds that an alternative facility with BSL-3 Enhanced (BSL-3E) and BSL-3Ag laboratory space will be needed to continue that research. However, **because foot-and-mouth disease research remains critical for the US animal health system, the committee concludes that it will be essential to support PIADC until an alternative facility is authorized, constructed, commissioned, and approved for work with FMDv (Conclusion 4).**

In evaluating the PIADC alternative, the committee spent a considerable amount of time examining the need for ABSL-4 large-animal laboratory space, how it would be used, and how much of it would be needed. Chapter 3 points out that although by definition none of the livestock-specific FADs requires

BSL-4 laboratory containment, a disease outbreak of a highly contagious zoonotic virus or a novel pathogen of undetermined transmissibility in US livestock would require appropriate biocontainment on an emergency basis. Research to characterize the infectious agent, validation of diagnostics, and studies of pathogenesis, virulence, shedding, transmission, and host range and susceptibility would need to be investigated in live animals.

As the committee explored the potential of relying on international partners for emergency work that might require ABSL-4 large-animal laboratory space, it found remarkably little capacity near the United States. In fact, space limitations at the Canadian biocontainment facility in Winnipeg, Manitoba, have resulted in a project to expand the capacity for ABSL-4 large-animal containment there. The committee notes that it is in the interest of the United States to actively pursue partnerships with countries that have ABSL-4 large animal laboratories to study known zoonotic agents of agricultural concern. However, given the uncertainty over priorities of a foreign laboratory and logistical difficulties in an emergency, it would not be desirable for the United States to rely on international laboratories to meet ABSL-4 large-animal needs in the long term. Therefore, **as part of the national infrastructure for protecting animal and public health, the committee concludes that there is an imperative to build ABSL-4 large-animal space in the United States (Conclusion 5).**

A key question is whether cost savings would be realized by reducing the scope and capacity of an NBAF and performing some functions elsewhere. As noted in Chapter 4, the committee was provided limited and insufficient information to assess the actual costs of this scaled-back option (which included reductions in the currently planned space for building support and BSL-3Ag, BSL-3E, and BSL-4 space). The DHS staff asserted that any redesign of the current plan for the NBAF, even a reduction in size, would add to its cost. The committee was surprised that DHS had no contingency plan for a building of reduced size in the event of budget cuts. Moreover, the committee found a sizable discrepancy between costs projected for constructing the proposed NBAF and costs associated with other recently constructed biocontainment facilities. The committee did recognize that part of the discrepancy in construction costs results from the recommendations to “harden” the proposed facility because of concerns about the building's structural integrity for the proposed site. But there is not a good estimate of operating costs for the streamlined scenario.

A partnership of a central national laboratory of reduced scope and size and a distributed laboratory network could effectively protect the United States from FADs and zoonotic diseases, potentially realize cost savings, reduce redundancies, and enhance the cohesiveness of a national system of biocontainment laboratories. However, because the cost implications of reducing the scope and capacity of a central facility cannot be known without further information and study, it will be important for DHS to make a good-faith effort to re-examine construction and operating costs of a laboratory of reduced size and complexity.

CONSIDERATIONS FOR FULFILLING NATIONAL NEEDS

Realizing cost savings in the construction and operation of laboratory facilities is a critically important objective. However, it is no less important for DHS, the US Department of Agriculture (USDA), and other relevant agencies to maintain their focus on the overarching goal of developing a highly capable system for addressing FAD and zoonotic disease threats. A central laboratory would be a key part of an integrated national system, but it would only be one component of the system; therefore **the committee concludes that innovative, forward-thinking solutions are required not only about the central laboratory but about the entire system (Conclusion 6)**. The solutions for the entire system may need to involve consideration of a wider range of options for the central laboratory. That analysis extends beyond the scope of the current study.

As described in previous chapters, the ideal system to counter threats from FADs and zoonotic diseases includes research, development, and training; a centralized core facility; a distributed network of national and international partnerships; and disease surveillance, diagnostic, and response capabilities. In exploring national capabilities, the committee found a substantial number of public and private biocontainment laboratories across the country; these are capabilities that did not exist nearly a decade ago when Homeland Security Presidential Directive 9 was issued. Chapter 3 provides a map and a list of institutions that house a variety of BSL-3, BSL-3Ag, and BSL-4 laboratories in the United States. It is reasonable to view those facilities as potential partners in a national system and to expect that those existing capabilities can be leveraged in the national interest. The major barriers to leveraging capabilities at those facilities are the need to establish formal relationships, agreed-upon operational protocols, contractual funding arrangements, and well-reasoned policies about the kind of work that can be conducted in different facilities. Yet in the committee's view, it is precisely those kinds of relationships that could move the nation closer to the ideal, integrated national system to address animal disease threats—one in which a distributed laboratory network is tied closely to a central supporting facility. **Regardless of the options considered for a central facility, the committee recommends that DHS and USDA develop and implement an integrated national strategy that utilizes a distributed system for addressing FAD and zoonotic disease threats (Recommendation)**. The National Animal Health Laboratory Network (NAHLN) is an excellent model of such a distributed network of laboratories and would serve a critical role in a more comprehensive and integrated national strategy.

Balanced Support for Infrastructure and Research and Development

The committee concludes that it is critical for policy-makers and agency planners to recognize that an effective system for addressing FAD and zoonotic disease threats to the United States consists of more than facilities;

it also requires robust research programs (Conclusion 7). Those cannot be traded off against one another; rather, balanced support is needed to sustain research priorities and capital costs associated with maintaining or constructing modern laboratory facilities. The United States is fortunate to have significant physical and intellectual assets, both in government and in universities, which could be better used and coordinated to support a national research strategy. In deciding the best path forward, it will be critical for DHS and USDA to consider a holistic approach for developing solutions, one that strikes a balance between facilities costs and the research and development effort needed to protect American agriculture and public health.

Ongoing Planning and Prioritizing for the National System

The committee concludes that conceptualizing, implementing, and maintaining a US national system to address threats posed by FADs and zoonotic diseases requires not only an understanding of today's priorities and technologies but continued monitoring and assessment to understand how the high-priority threats and the tools available to address them change over time. Such vision and planning are critical and must be ongoing (Conclusion 8). There is a related need for continuing communication and coordination among the many parties and stakeholders that form an efficient, effective, and integrated national system. The central facility network of national laboratory partnerships will require coordination not only in selecting national disease priorities and determining how those priorities should evolve, but in establishing the practical agreements and other details that would enable such a system to function. One possible mechanism to address some of those needs may be the establishment of a council that engages key stakeholders and is analogous to the model of the NAHLN Coordinating Council.

Alternative Funding Mechanisms

The committee concludes that exploring alternative funding mechanisms to supplement current federal allocations for capital and operational costs and for program support would be useful (Conclusion 9). Alternative funding strategies used by other countries could be considered as possible models. For instance, Australia draws on industry contributions to help support its national animal disease capabilities. It may also be useful to explore the possibility of using public-private partnerships to support and maintain aspects of facilities and research programs.

Consideration of All Factors of Concern

The importance of having a strong national system to recognize and counter the threats posed by FADs and zoonotic diseases may not always be apparent

when disease outbreaks are quickly identified, mitigated, and contained, but the consequences of such disease outbreaks can be enormous if and when a system fails. This study provides a high-level view of whether each of the three options stipulated by DHS could be feasible in meeting the nation's needs. As discussed in Chapter 4, the committee also recognizes that the three DHS-proposed options may not be the only options worth considering. Concerns considered in this study—costs, necessary capabilities, and infrastructure needs—do not reflect all of the factors decision-makers must consider. The factors that were considered in the original assessment that led to decisions about the NBAF may or may not have changed. For example, safety concerns still linger on the issue of bringing foot-and-mouth disease research onto the US mainland and the risk of accidental release of FMDv and its consequent impacts (NRC, 2010, 2012). Decisions about infrastructure needs should not be made in the absence of risk concerns as well as the many other factors worthy of consideration. **The committee concludes that to most appropriately fill critical laboratory needs in the United States, all factors of concern (including site location, risk assessment, political considerations, adaptability for the future) will need to be considered in a more comprehensive assessment (Conclusion 10).**

REFERENCES

- NRC (National Research Council). 2010. Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas. Washington, DC: The National Academies Press.
- NRC. 2012. Evaluation of the Updated Site-Specific Risk Assessment for the National Bio- and Agro-Defense Facility in Manhattan, Kansas. Washington, DC: The National Academies Press.

Appendixes

Appendix A

Committee Biosketches

Terry F. McElwain (*Chair*) is the executive director of the Washington Animal Disease Diagnostic Laboratory and the associate director of the Paul G. Allen School for Global Animal Health in the College of Veterinary Medicine of Washington State University. He is past president of the American Association of Veterinary Laboratory Diagnosticians and serves on the Board of Directors of the World Association of Veterinary Laboratory Diagnosticians. Dr. McElwain has been a key architect of the creation and development of the National Animal Health Laboratory Network and has been closely involved in the development of the School for Global Animal Health at Washington State University. He interacts with the Centers for Disease Control and Prevention and is a member of the Washington governor's emergency preparedness task force. He has served on the National Research Council Committee on Assessing the Nation's Framework for Addressing Animal Diseases and Committee for Achieving Sustainable Global Capacity for Surveillance and Response to Emerging Diseases of Zoonotic Origin. Dr. McElwain has a long record of research in veterinary infectious diseases, especially those of agricultural animals. He received his DVM from the College of Veterinary Medicine of Kansas State University and his PhD from Washington State University. He is a member of the Institute of Medicine.

Nancy D. Connell is a professor in the Division of Infectious Disease of the Department of Medicine of the University of Medicine and Dentistry of New Jersey (UMDNJ) New Jersey Medical School. Dr. Connell's major research focus is the interaction between respiratory infectious agents and the macrophage. She is director of the biosafety level 3 facility of UMDNJ's Center for the Study of Emerging and Re-emerging Pathogens and chairs the university's Institutional Biosafety Committee. Dr. Connell is a past chair of the Center for Scientific Review Study Section at the National Institutes of Health that reviews bacterial-pathogenesis submissions to the National Institute of Allergy and Infectious Diseases and of the study section that reviews fellowships in infectious diseases and microbiology. She now serves on study sections that focus on anti-

bacterial drug discovery and innate immunity. Dr. Connell's interest in biological-weapons research and policy issues began in the 1980s, when she chaired a subcommittee on biological weapons of the Council for Responsible Genetics. She has served on a number of committees of the National Research Council, including the Committee on Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Agents (2006), the Committee on Trends in Science and Technology Relevant to the Biological Weapons Convention: An International Workshop (Beijing, China [2011]), and the Committee on Review of the Scientific Approaches Used during the FBI's Investigation of the 2001 *Bacillus anthracis* Mailings (2011). Dr. Connell received her PhD in microbiology from Harvard University.

David Hennessy is a professor in the Department of Economics and the Center for Agricultural and Rural Development, both at Iowa State University. His research program emphasizes risk management, food quality and the provision of safe food, animal disease economics, agricultural structure, and roles of information in farm-level production decisions. His program on animal disease deals with risks and biosecurity incentives. Issues addressed have included the role of feeder animal trade in determining the ambient level of an infectious disease, biosecurity choices in light of the dynamics of disease incidence, costly regulation in the face of scientific uncertainty, managing disease when infection externalities arise, and how interdependent participation incentives can be used to ensure the success of voluntary livestock disease control programs. His teaching responsibilities concern commodity market analysis, business economics, agribusiness management, demand and supply systems, and decision analysis. Before joining the faculty at Iowa State University, Dr. Hennessy was on the faculty at Washington State University. He is a Fellow of the Agricultural and Applied Economics Association and currently serves as an editor of the *American Journal of Agricultural Economics*. Dr. Hennessy received his bachelor's and master's degrees in Agricultural Science from University College Dublin, and his PhD in Agricultural Economics from Iowa State University.

Lonnie J. King is dean of the College of Veterinary Medicine and executive dean for the Health Science Colleges of Ohio State University. Previously, Dr. King was the director of the National Center for Zoonotic, Vector-Borne, and Enteric Diseases at the Centers for Disease Control and Prevention (CDC). Before serving as director, he was the first chief of CDC's Office of Strategy and Innovation. Dr. King served as the 11th dean of the Michigan State University College of Veterinary Medicine for 10 years. Before that, he was the administrator of the Animal and Plant Health Inspection Service of the US Department of Agriculture. He served as the country's chief veterinary officer for 5 years and worked extensively in global trade agreements within the North American Free Trade Agreement and the World Trade Organization. He has served as president of the Association of American Veterinary Medical Colleges and was the vice-chair of the National Commission on Veterinary Economic Issues. Dr. King

received his BS and DVM from Ohio State University and his MS in epidemiology from the University of Minnesota; he also received an MPA from American University. He is a member of the Institute of Medicine.

James W. Le Duc directs the Galveston National Laboratory of the University of Texas Medical Branch. He also serves as a professor in the Department of Microbiology and Immunology in the School of Medicine. Previously, he served as the coordinator for influenza for the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and was the director of the Division of Viral and Rickettsial Diseases in the CDC National Center for Infectious Diseases (NCID). He began his professional career as a field biologist with the Smithsonian Institution's African Mammal Project in West Africa. He then served for 23 years as an officer in the US Army Medical Research and Development Command. He joined CDC in 1992, was assigned to the World Health Organization as a medical officer, and later became the associate director for global health at NCID. His research interests include the epidemiology of infectious diseases, global health, and international biosecurity. He is a member of various professional organizations, has published over 200 scientific articles and book chapters, and is an expert in viral diseases, biodefense, and global health. Dr. Le Duc earned his PhD and MSPH from the University of California, Los Angeles and his BS in zoology from California State University.

N. James Maclachlan is a Distinguished Professor in the Department of Pathology, Microbiology and Immunology in the School of Veterinary Medicine of the University of California (UC) at Davis and Extraordinary Professor in the Department of Veterinary Tropical Diseases Faculty of Veterinary Science of the University of Pretoria in the Republic of South Africa. Dr. Maclachlan is a diplomate and past president of the American College of Veterinary Pathologists, and he served for 10 years as inaugural chair of his home department at UC Davis. He studies viral diseases of livestock that affect international commerce, including bluetongue, African horse sickness, and other emerging diseases, and he is author or coauthor of some 250 peer-reviewed publications, reviews, chapters, and books. Dr. Maclachlan has served as an expert adviser to numerous organizations, including the World Organisation for Animal Health, the US Department of Agriculture and Department of Homeland Security, and the European Union. Among other responsibilities, he chairs the United States Animal Health Association Committee on Bluetongue and Related Orbiviruses and serves as co-editor-in-chief of *Comparative Immunology, Microbiology & Infectious Diseases*. He received his BVSc from Massey University in New Zealand, his MS in microbiology (virology) from the University of Missouri, and his PhD in comparative pathology from UC Davis.

Bret D. Marsh serves as the Indiana state veterinarian. He is responsible for all statewide animal health programs and provides inspection services for the meat, poultry, and dairy products industries. He is also an adviser to the Indiana Board of Veterinary Medical Examiners. Dr. Marsh previously served as the special detail to the US Secretary of Agriculture's Homeland Security Staff, representing the views of the country's state veterinarians on issues affecting the nation's ability to preserve and protect its agricultural assets. He recently completed a 6-year term as the American Veterinary Medical Association (AVMA) treasurer and also served in the AVMA House of Delegates for nearly a decade. In that time, he was twice elected to the House Advisory Committee and served on the Constitution and Bylaws Committee. Dr. Marsh is a past president of the Indiana Veterinary Medical Association (IVMA), the United States Animal Health Association (USAHA), and the Purdue Veterinary Alumni Association. He has received the Distinguished Alumnus Award from both the Purdue College of Veterinary Medicine and the Purdue College of Agriculture. He has also received the AVMA President's Award, the USAHA Medal of Distinction, and the IVMA President's Award. He received his BS in animal sciences and his DVM from Purdue University.

Mo Salman is a professor of veterinary epidemiology in the Animal Population Health Institute of Colorado State University's College of Veterinary Medicine and Biomedical Sciences. He holds appointments in the Department of Clinical Science and the Department of Environmental Health and Radiological Sciences. Dr. Salman's educational background is in veterinary medicine, preventive veterinary medicine, and comparative pathology. He received his veterinary medical degree from the University of Baghdad, Iraq, and a master's degree in preventive veterinary medicine and a PhD from the University of California at Davis. He is a diplomate of the American College of Veterinary Preventive Medicine and a fellow of the American College of Epidemiology. Dr. Salman is engaged in research and outreach projects in more than 15 countries. He participated in the peer review of the European Union scientific review for the geographic assessment for bovine spongiform encephalopathy and was elected to the European Food Safety Agency's Panel for Animal Health and Welfare. He is the chairman of the Continuing Education Committee of the Association for Veterinary Epidemiology and Preventive Medicine. He is the recipient of the 2007 American Veterinary Medical Association XII International Veterinary Congress Prize for his contributions to international understanding of veterinary medicine. In 2011, Dr. Salman was selected to serve a 4-year appointment on the Scientific Advisory Board of the Friedrich-Loeffler-Institut, the federal research institute for animal health in Germany, which is an independent research entity that focuses on the health of farm animals and protection of humans from zoonoses. Dr. Salman's research interests are in methods of surveillance of animal diseases with an emphasis on infectious diseases.

Alfonso Torres is a professor in the College of Veterinary Medicine of Cornell University, where he also serves as associate dean for veterinary public policy. He coordinates international programs and academic initiatives in public health. Before his return to academe in 2002, he served in the US Department of Agriculture (USDA) for 11 years, where he was involved in activities related to protecting our nation against the incursion of foreign animal diseases. He was the director of the Plum Island Animal Disease Center before serving USDA as chief veterinary officer. During 2001, Dr. Torres worked closely with Secretary of Agriculture Veneman on efforts to prevent the entry of foot-and-mouth disease (FMD) into the United States. He also served as the US delegate to the World Organisation for Animal Health in matters related to international standards for the trade of animals and animal products. Those activities provided him with the opportunity to participate with other federal officials in international trade negotiations related to our import and export of animals and animal products. He was one of the lead participants at USDA in preparing a comprehensive report to a Senate committee as part of the Animal Disease Risk Assessment, Prevention, and Control Act of 2001 (PL 107-9), which was concerned with the plans of federal agencies to defend our country against FMD and bovine spongiform encephalopathy. Dr. Torres received his DVM from the National University of Colombia in Bogota, his MS in veterinary pathology and PhD in medical microbiology from the University of Nebraska-Lincoln.

Christopher A. Wolf is a professor of agricultural, food, and resource economics at Michigan State University (MSU). His research and outreach program focuses on farm management, markets, and policy. His recent work examines the economics of livestock and wildlife disease management and behavioral incentives provided to producers by current policies. Dr. Wolf was awarded the Excellence in Outreach Award by the MSU Department of Agriculture, Food, and Resource Economics in 2008. He is a member of the Agricultural & Applied Economics Association and was part of its Distinguished Extension Program-Group, 2000 in 2010. He was domain leader (2007–2009) of the Farm Business Management Section of DAIREXNET, a national, extension-driven Web resource designed to meet the educational and decision-making needs of dairy producers, allied-industry partners, extension educators, and consumers. He received his BA from the University of Wisconsin-Madison and his PhD in agricultural and resource economics from the University of California at Davis.

Appendix B

Meeting Agendas

FIRST COMMITTEE MEETING

Keck Center of the National Academies
Washington, DC

Friday, April 13, 2012

- 9:15 a.m. **Welcome, Chair Opening Remarks**
Terry McElwain, Committee Chair
- Opening Remarks from the U.S. Department of Homeland Security (DHS)**
Tara O'Toole, DHS Under Secretary for Science and Technology
- Committee Member Introductions**
Terry McElwain, Committee Chair
- 9:30 a.m. **Statement of Task and Expectations from the NRC Study**
James Johnson, Director, Office of National Labs, DHS S&T
- Background & Threat Environment**
James Johnson, Director, Office of National Labs, DHS S&T
- 10:00 a.m. *Coffee Break*
- 10:10 a.m. **Programs at PIADC and Program Planned for NBAF**
Steve Kappes, Deputy Administrator, Animal Production & Protection, USDA-ARS

120 *CRITICAL LABORATORY NEEDS FOR ANIMAL AGRICULTURE*

Elizabeth Lautner, Director, National Veterinary Services
Laboratory, USDA-APHIS

Michelle Colby, Chief, Agricultural Defense Branch, DHS
Larry Barrett, Director, Plum Island Animal Disease Center, USDA

Current State of PIADC

James Johnson, Director, Office of National Labs, DHS S&T

NBAF Site Plan, Laboratory Design, Construction, Schedule

James Johnson, Director, Office of National Labs, DHS S&T

- 11:30 a.m. **Friedrich-Loeffler-Institut Capacity and Capabilities**
(Via Videoconference)
Thomas Mettenleiter, President, Friedrich-Loeffler-Institut
Federal Research Institute for Animal Health, Island of Riems,
Greifswald, Germany
- 12:00 p.m. **Lunch**
- 1:00 p.m. **Additional Program Information**
James Johnson, Director, Office of National Labs, DHS S&T
- 1:30 p.m. **Canadian National Centre for Animal Disease
Capacity and Capabilities** (Via Audioconference)
Soren Alexandersen, Director, The National Centre for Animal
Disease, Canadian Food Inspection Agency, Winnipeg, Canada
- 2:00 p.m. **CDC BSL-4 Laboratory and Microbial Threats**
Pierre Rollin, Team Leader, Special Pathogens Branch,
Centers for Disease Control and Prevention
- 2:30 p.m. **The KSU BSL-3 Biosecurity Research Institute
Capacity and Capabilities, Future Plans for Additional Work**
Stephen Higgs, Director, Biosecurity Research Institute,
Kansas State University
- 3:00 p.m. **Coffee Break**
- 3:15 p.m. **Q & A** with all speakers

- 4:00 p.m. **Australian Animal Health Laboratory Capacity and Capabilities** (Via Audioconference)
Martyn Jeggo, Director, Australian Animal Health Laboratory,
The Commonwealth Scientific and Industrial Research
Organisation, Victoria, Australia
- 4:30 p.m. **Open Microphone for Public Comments**
Each speaker has a maximum time of 5 minutes.
- 5:00 p.m. **Adjourn Open Session**

TELECONFERENCES

Wednesday, May 2, 2012

- 3:00 p.m. **Opening remarks, committee introductions**
Terry McElwain, Committee Chair
- 3:05 p.m. **Information about the Department of Homeland Security National BioDefense Analysis and Countermeasures Center (NBACC)**
Patrick Fitch, NBACC Laboratory Director
Jim Swearingen, NBACC Director of Comparative Medicine
- 4:00 p.m. **Adjourn phone call**

Thursday, May 3, 2012

- 2:00 p.m. **Opening remarks, committee introductions**
Terry McElwain, Committee Chair
- 2:05 p.m. **Information about the United States Army Medical Research Institute for Infectious Disease (USMRIID)**
Neal Woollen, USAMRIID Director of Safety, Security,
and Biosurety
Leonard Smith, USAMRIID Senior Research Scientist for
Medical Countermeasures Technology
- 3:00 p.m. **Adjourn phone call**

122 *CRITICAL LABORATORY NEEDS FOR ANIMAL AGRICULTURE*

Friday, May 4, 2012

- 2:00 p.m. **Opening remarks, committee introductions**
Terry McElwain, Committee Chair
- 2:05 p.m. **Information about the Rocky Mountain Laboratories**
Kathryn Zoon, NIAID Director of the Division of
Intramural Research
- 3:00 p.m. **Adjourn phone call**

Appendix C

Brief History of the Plum Island Animal Disease Center

The development of biocontainment facilities for the study of animal diseases is historically associated with the need to provide diagnostic and research capabilities to deal with a potential outbreak of foot-and-mouth disease in the United States.

There have been nine outbreaks of foot-and-mouth disease in the United States: in 1870 in New England and New York; in 1880 (in imported animals controlled before release of the animals); in 1884 in Maine; in 1902 in Massachusetts, New Hampshire, Rhode Island, and Vermont; in 1908 in Maryland, Michigan, New York, and Pennsylvania; in 1914 (the most extensive outbreak) in the District of Columbia and 22 states—Connecticut, Delaware, Illinois, Indiana, Iowa, Kansas, Kentucky, Maryland, Massachusetts, Michigan, Minnesota, Montana, New Hampshire, New Jersey, New York, Ohio, Pennsylvania, Rhode Island, Virginia, Washington, West Virginia, and Wisconsin; in 1924 in California; in 1924 in Texas; and in 1929 in California.

During those years, diagnosis of foot-and-mouth disease was based on experimental animal inoculations in affected areas in the field. No laboratory work with foot-and-mouth disease virus was permitted in the United States after the eradication of the last cases in 1929.

In December 1946, foot-and-mouth disease type A was diagnosed for the first time in Mexico in the state of Veracruz. On February 28, 1947, Public Law (PL) 80-8 (S. 568) authorized the Secretary of Agriculture to cooperate with the government of Mexico in the control and eradication of foot-and-mouth disease. A cooperative program started on March 27, 1947. Early in the campaign, it was necessary to use vaccination for the control of foot-and-mouth disease. Vaccine was first purchased from Europe because all vaccines from South America were of types O and C. Later, the vaccine was produced in Mexico. These foot-and-

mouth disease research activities demonstrated the need to have biosecure laboratories in the United States where this type of research could be conducted.

A few years before the Mexican outbreak, the US Department of Agriculture (USDA) had established a robust research program on foot-and-mouth disease and other foreign animal diseases through cooperative agreements with foreign laboratories, particularly those at the Foot-and-Mouth Disease Research Institute in Pirbright, England; the State Veterinary Research Institute in Amsterdam, Holland; the Danish Foot-and-Mouth Disease Research Institute in Lindholm, Denmark; and the Swiss Federal Vaccine Institute in Basel. Each of those laboratories hosted one or two USDA scientists. However, Congress and the animal industries felt that the research based in foreign laboratories was inadequate for US needs and prompted discussions about the authorization of the establishment of a laboratory in the United States “to conduct research on foot-and-mouth disease and other diseases of animals” (PL 80-496 (Sec. 2038)), which culminated in the approval of PL 80-496 on April 24, 1948. The law provided an annual operating budget of \$3 million “to cover employment of 50 trained scientists, 200 people to handle the animals, and 200 employees of various classes; animals to conduct the experiments (including 1,200 cattle); and supplies, materials and travel” (S. Rep. No. 211, 80th Cong., 2d Sess. (1948)). Congress also required laboratory safety conditions more stringent than those in the European foot-and-mouth disease laboratories, following standards developed by the National Institutes of Health laboratories in Bethesda, Maryland, ensuring that all animal experimentation would take place in completely enclosed animal rooms isolated from each other.

To implement PL 80-496, Congress approved the use of up to \$30 million for the entire cost of establishment of a foot-and-mouth disease laboratory by USDA’s Bureau of Animal Industries to be

a coastal island separated from the mainland by deep, navigable water and not connected with the mainland by a tunnel... [with a] continuous supply of hundreds of thousands of gallons of fresh water daily... [and with] transportation facilities from the mainland for personnel, animals, and materials, uninterrupted by weather conditions (S. Rep. No. 211, 80th Cong., 2d Sess. (1948)).

It should be noted that in 1990 (PL 101-624), Congress amended the original restrictions for working with live foot-and-mouth disease virus on the US mainland by declaring that such work was prohibited

unless the Secretary determines that it is necessary and in the public interest for the conduct of research and study in the United States (except at Brookhaven National Laboratory in Upton, New York) and issues a permit under such rules as the Secretary shall promulgate to protect animal health...(21USC§113a).

In 2008 (PL 110-234), the foot-and-mouth disease restrictions were amended again to authorize the Secretary of Agriculture to issue a permit to the Secretary of Homeland Security

for work on the live virus of foot and mouth disease at any facility [with a limit of only one facility] that is a successor to the Plum Island Animal Disease Center and charged with researching high-consequence biological threats involving zoonotic and foreign animal diseases...(PL 110-234, Title VII § 7524, May 22, 2008, 122 Stat. 1273).

The search for a suitable location for a foot-and-mouth disease research facility turned out to be a difficult task because of the site restrictions imposed by the Congressional language, and the process lingered until the appearance in 1952 of the first (and only) outbreak of foot-and-mouth disease in Saskatchewan, Canada. At that time, the US Army Chemical Corps had initiated the renovation of buildings at Fort Terry, located on Plum Island, New York, to conduct chemical and biological research. Fort Terry had been in use by the Army since 1897 as an artillery coastal defense post. Eighteen buildings from the Fort Terry days were renovated by the Army Chemical Corps, including the Combined Torpedo Storehouse and Cable Tanks (circa 1911) building, later known as Building 257, to conduct biological experiments.

In 1952, the Army decided to suspend operations at Fort Terry and to transfer Plum Island to USDA's Bureau of Animal Industries. USDA scientists moved to the renovated Building 257 in 1953. Building of a new facility, to be known as Building 101, started on July 1, 1954, and the building was dedicated on September 26, 1956. The Plum Island Animal Disease Center (PIADC) was inaugurated; it occupied the new building, and the 18 Fort Terry-era buildings were renovated by the Army.

In 1977, as PIADC was aging, a master plan for its modernization was completed. The plan included the construction of new facilities to house most of the functions that were in the repurposed Fort Terry post buildings and batteries. Much of the plan never materialized.

In 1984, the diagnostic and training missions of PIADC were transferred from the USDA Agricultural Research Service (ARS) to the USDA Animal and Plant Health Inspection Service (APHIS). The new unit, the Foreign Animal Disease Diagnostic Laboratory (FADDL), became one of the National Veterinary Services Laboratories. Most of the FADDL activities were confined to Building 257. At that time, ARS and APHIS entered into a mutual support agreement to share the expenses of the operation and maintenance of the PIADC facilities, with ARS as the lead agency in charge of PIADC.

With the failure of the 1977 modernization plans, facilities remained essentially the same until a new study on facility modernization was developed in 1990. The age of Building 257 (over 80 years) and decreases in the number of research activities and personnel led to a modernization and consolidation of ARS and APHIS facilities, which was completed in 1995. As a result of the in-

frastructure investments, a new administration building (Building 100) was completed and inaugurated; it was attached to the front of Building 101. The project also resulted in the remodeling of nearly two-thirds of the laboratory space in Building 101 and the decommissioning of Building 257 and most of the Fort Terry-era buildings on the island. Buildings 100 and 101 still house all combined operations for APHIS, ARS, and now the Department of Homeland Security (DHS).

In October 1991, all operations and maintenance were privatized and transferred to a contractor under ARS supervision. In December 1994, an agreement was set in place to share leadership responsibility of PIADC by having the directorship cycle between ARS and APHIS every 5 years or on another agreed timetable. That agreement was never implemented, and ARS continued to provide the director until the transfer of PIADC to the newly formed DHS in June 2003. Today, DHS has oversight for administration and facility management and maintains operations of the facility in addition to having its own science program.