THE WHITE HOUSE

WASHINGTON

October 29, 2015

MEMORANDUM FOR DEPUTY SECRETARY OF STATE
DEPUTY SECRETARY OF DEFENSE
DEPUTY ATTORNEY GENERAL
DEPUTY SECRETARY OF THE INTERIOR
DEPUTY SECRETARY OF AGRICULTURE
DEPUTY SECRETARY OF TRANSPORTATION
DEPUTY SECRETARY OF COMMERCE
DEPUTY SECRETARY OF HEALTH AND HUMAN SERVICES
DEPUTY SECRETARY OF ENERGY
DEPUTY SECRETARY OF VETERANS AFFAIRS
DEPUTY SECRETARY OF HOMELAND SECURITY
DEPUTY ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY
PRINCIPAL DEPUTY DIRECTOR OF NATIONAL INTELLIGENCE
DEPUTY DIRECTOR OF THE NATIONAL SCIENCE FOUNDATION
ASSISTANT ADMINISTRATOR OF THE UNITED STATES AGENCY FOR INTERNATIONAL DEVELOPMENT
VICE CHAIRMAN OF THE JOINT CHIEFS OF STAFF
DEPUTY DIRECTOR OF THE FEDERAL BUREAU OF INVESTIGATION

SUBJECT: NEXT STEPS TO ENHANCE BIOSAFETY AND BIOSECURITY IN THE UNITED STATES

A national biosafety and biosecurity system is paramount to protecting the Nation's health, ability to conduct the highest quality research, national defense, and upholding public trust as the Federal government works to develop better means to prevent, detect, and respond to infectious disease threats around the world. Such goals are underscored by the *National Strategy for Countering Biological Threats* and the Administration's actions to implement its international elements under the Global Health Security Agenda (GHSA). Fostering and maintaining a strong culture of responsibility is vital to achieving such a system.

On August 18, 2014, we signed the memorandum attached at Tab A, which called for parallel Federal and broad stakeholder reviews to generate specific recommendations to strengthen the Federal Government's biosafety and biosecurity practices and oversight system. In response to that memorandum, the laboratory incidents that spurred it, as well as additional incidents, departments and agencies have developed implementation plans and timelines attached at Tab B, which have been reviewed and endorsed by the

Interagency Policy Committee (IPC) on Biological Select Agents and Toxins (BSAT).

These comprehensive stakeholder reviews resulted in a set of recommendations that address many of the factors associated with recent laboratory incidents in the United States.

The recommendations highlight the importance of stewardship and a culture of responsibility in the scientific and technical communities, including prioritization of biosafety and biosecurity. Implementing these recommendations, which have been developed by departments and agencies and endorsed by the IPC on BSAT, will strengthen the Federal Government's biosafety and biosecurity practices and its oversight system.

The recommendations and the accompanying implementation plans and timelines are consistent with the Administration's commitment to an effective national biosafety and biosecurity system under the *National Strategy for Countering Biological Threats* and the GHSA. In light of recent biosafety and biosecurity incidents, we urge swift implementation of these recommendations in order to enhance biosafety and biosecurity in the United States, highlighting the following:

1. **Transparency of the Nation's laboratory system for public safety and security**, particularly for those facilities that possess, use, or transfer BSAT, including identifying an approach to determine the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT so that the Nation's scientific, public and animal health, and national security needs can be met;

2. **Incident reporting and accountability to the public** for biosafety and biosecurity procedures, protocols, personnel reliability, and to ensure a culture of responsibility;

3. **Material stewardship**, including inventory management and control for facilities and personnel that possess, use, or transfer BSAT; and

4. **Applicability to other biological agents that could pose a serious threat to public health or agriculture:** The three principles above should also be applied to encompass transparency, enhanced incident reporting and accountability, and material stewardship, including inventory management and control, for any biological agent

that could pose a serious threat to public health or agriculture.

The National Security Council staff and the Office of Science and Technology Policy will conduct implementation reviews on a semi-annual basis. We also encourage departments and agencies to share lessons learned with international partners and to update implementation plans on a continual basis given advances in science and technology. Thank you for your swift attention to these important actions.

Lisa O. Monaco
Assistant to the President for Homeland Security and Counterterrorism

John P. Holdren
Assistant to the President for Science and Technology

Attachments

Tab A	Memorandum, "Enhancing Biosafety and Biosecurity in the United States" (August 18, 2014)
Tab B	Recommendations, implementation plans, and timelines for enhancing biosafety and biosecurity in the United States
Tab C	FESAP report
Tab D	FTAC report

Tab A

THE WHITE HOUSE

WASHINGTON

August 18, 2014

MEMORANDUM FOR DEPUTY SECRETARY OF STATE
DEPUTY SECRETARY OF DEFENSE
DEPUTY ATTORNEY GENERAL
DEPUTY SECRETARY OF AGRICULTURE
DEPUTY SECRETARY OF TRANSPORTATION
DEPUTY SECRETARY OF COMMERCE
DEPUTY SECRETARY OF HEALTH AND HUMAN SERVICES
DEPUTY SECRETARY OF ENERGY
DEPUTY SECRETARY OF VETERANS AFFAIRS
DEPUTY SECRETARY OF HOMELAND SECURITY
DEPUTY ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY
PRINCIPAL DEPUTY DIRECTOR OF NATIONAL INTELLIGENCE
DEPUTY DIRECTOR OF THE NATIONAL SCIENCE FOUNDATION
DEPUTY DIRECTOR OF INTERIOR
ASSISTANT ADMINISTRATOR OF THE UNITED STATES AGENCY FOR INTERNATIONAL DEVELOPMENT
VICE CHAIRMAN OF THE JOINT CHIEFS OF STAFF
DEPUTY DIRECTOR OF THE FEDERAL BUREAU OF INVESTIGATION

SUBJECT: ENHANCING BIOSAFETY AND BIOSECURITY IN THE UNITED STATES

It is essential for the United States Government to conduct life sciences research to prevent, detect, and respond to infectious disease threats posed by natural events or deliberate acts of bioterrorism. It is also the government's responsibility to ensure that infectious disease research in the United States is conducted safely and securely. The United States Government has acted swiftly to address three recent U.S. biosafety and biosecurity incidents. To improve U.S. preparedness for such threats and incidents, it is imperative that infectious disease researchers: (1) conduct a comprehensive review of current biosafety and biosecurity protocols and procedures to ensure they are adequate and appropriate for today's infectious disease research; (2) inventory and document their culture collections; and (3) increase attentiveness throughout the research community

to ensure the safety of laboratory researchers and the American public. To maximize the positive effect of lessons learned from the recent incidents, we are urging all United States Government departments and agencies that work with infectious agents to take immediate and long-term steps to enhance safety and security of research to minimize the potential for future incidents. While immediate action is necessary, United States Government departments and agencies are also urged to continuously review, implement and where appropriate, refine sustainable stewardship practices for biosafety and biosecurity.

Immediate Steps:

- Within 30 days of the release of this memorandum, all United States Government departments and agencies that operate facilities that possess, use, or transfer human, animal, or plant infectious agents or toxins are urged to perform a "Safety Stand-Down." During the Safety Stand-Down period, senior leaders will devote significant, dedicated time to review laboratory biosafety and biosecurity best practices and protocols, as well as to develop and implement plans for sustained inventory monitoring. Senior leaders should confer with local and agency management and staff to identify opportunities for improving research safety and local oversight systems. In practical terms, this review may take place over several days to ensure that scientific endeavors and clinical care are not adversely affected and to permit safe and efficient laboratory management. Leaders should use this Safety Stand-Down to kick-off an immediate sweep of their facilities that possess, use, or transfer human, animal, or plant infectious agent or toxin holdings to identify Biological Select Agents and Toxins (BSAT)[1] and ensure their proper registration, safe stewardship, and secure storage or disposal [Tab A][2]. United States Government departments and agencies have agreed to complete this sweep by October 1, 2014.

---

[1] See 42 CFR §§ 73.3, 73.4; 9 CFR §§ 121.3, 121.4; and 7 CFR § 331.3

[2] In accordance with Federal regulations (*see* 42 CFR §§ 73.5, 73.6, 73.9; 9 CFR §§ 121.5, 121.6, 121.9; and 7 CFR §§ 331.5, 331.9), departments and agencies will notify the appropriate authorities if any BSAT is located out of regulatory control. Any identified BSAT that requires movement will be reported to the Federal Select Agent Program in accordance with Federal regulations (see http://www.selectagents.gov/CDForm.html), transferred in accordance with Federal regulations (see http://www.selectagents.gov/TransferForm.html); and, where appropriate, transported in accordance with Department of Transportation Hazardous Material Regulations (49 C.F.R. parts 171-180.)

- Extramural facilities receiving United States Government funding that possess, use, or transfer human, animal, or plant infectious agents or toxins are encouraged to hold similar events and should be supported in these activities by United States Government departments and agencies to the greatest extent possible, such as by providing instructional materials on safety and security best practices. Departments and agencies providing funding to extramural facilities have agreed to coordinate to provide uniform guidance.

- Department and agency officials who are responsible for oversight of infectious disease research programs or who have safety oversight responsibilities, but are not part of a laboratory facility, are urged to participate in the Safety Stand-Down to demonstrate their commitment, and that of their organization, to safety and security.

- Departments and agencies are urged to provide written documentation of activities taken in support of the aforementioned objectives to the Interagency Policy Committee on BSAT by October 15, 2014. Departments and agencies are urged to provide progress reports, including any identified corrective actions or barriers to success, to National Security Council (NSC) and Office of Science and Technology Policy (OSTP).

Longer-Term Efforts to Improve Biosafety and Biosecurity Measures:

To strengthen United States Government oversight for work with pathogens, including BSAT, we are establishing parallel Federal and non-Federal reviews that will result in specific recommendations to strengthen the government's biosafety and biosecurity practices and oversight system for Federally funded activities, consistent with the need to realize the public, animal, and plant health and security benefits of such work. These United States Government-wide reviews will be coordinated with reviews initiated independently by the Department of Health and Human Services.

- Federal: United States departments and agencies have agreed to conduct a coordinated Federal review through an existing interagency committee to identify needs and gaps and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT and identify actions and any regulatory changes necessary to improve biosafety and biosecurity. The committee will build on

recommendations from previous reports made by and for the Federal government on biosafety and biosecurity, corrective actions identified as a result of the Safety Stand-Down, and the after-action assessments from the three recent U.S. biosafety and biosecurity incidents. The committee will also identify an approach to determine the appropriate number of high-containment U.S. laboratories required to possess, use, or transfer BSAT. United States Government departments and agencies have agreed that the committee will provide a set of recommended actions to the Assistant to the President for Homeland Security and Counterterrorism and the Assistant to the President for Science and Technology within 90 days of the receipt of this tasking.

- Broad Stakeholder Engagement: In response to the three recent U.S. biosafety and biosecurity incidents, the National Science and Technology Council (NSTC) will establish an interagency group to conduct a comprehensive review of the impact that the Select Agent Regulations (SAR) have had on science, technology, and national security. The group should include in its review an analysis of benefits, costs, and limitations of the SAR, as well as offer recommendations to address any identified challenges or gaps. To support this process, the NSTC will convene a public meeting of SAR stakeholders to inform and support the NSTC-led process. The NSTC body will be identified or created within 30 days of the date of this memorandum and will provide recommendations directly to the Assistant to the President for Science and Technology within 180 days of identification.

- Global: The United States will promote transparency concerning the recent biosafety and biosecurity incidents. This will include:
  - Developing a clear and consistent message to international partners for deployment bilaterally by individual agencies and programs, which deliver biological assistance. This message will describe U.S. biorisk management "lessons learned" and highlight the prompt U.S. action taken to address the recent U.S. biosafety and biosecurity incidents;
  - Utilizing multilateral venues, including the Global Health Security Agenda (GHSA), the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, and the Biological Weapons Convention, to promote transparency, address potential international concerns, and, as appropriate, encourage similar actions; and

- In the context of the GHSA, the United States will commit to achieve domestically the objective, "Promoting national biosafety and biosecurity systems," consistent with the target that we have set for our international engagement to include:
  1. A whole-of-government national biosecurity system is in place that ensures collections of especially dangerous pathogens are identified, held, secured and monitored in a minimal number of facilities with biosafety and biosecurity best practices in place;
  2. Biorisk management training and educational outreach is conducted to promote a shared culture of responsibility, reduce dual use biological risks and ensure safe transfer of biological agents; and
  3. Country-specific biosecurity legislation, laboratory certification, and pathogen control measures are in place, as appropriate.

Lisa O. Monaco
Assistant to the President for Homeland Security and Counterterrorism

John P. Holdren
Assistant to the President for Science and Technology

Attachment
Tab A Guidance on Select Agent Reporting

cc:
Assistant to the President and Counsel to the President
Assistant to the President and Deputy Chief of Staff for Policy
Assistant to the President and Director of the Domestic Policy Council
Assistant to the President and Director of the Office of Legislative Affairs
Deputy Assistant to the President and National Security Advisor to the Vice President
Associate Director for National Security Programs of the Office of Management and Budget

Federal Select Agent Program

Select Agents are Reportable

Select Agents and Toxins

Abrin
Botulinum neurotoxins
Botulinum neurotoxin producing species of *Clostridium*
Conotoxins (Short, paralytic alpha conotoxins)
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus[1]
Ebola virus
Francisella tularensis
Lassa fever virus
Lujo virus
Marburg virus
Monkeypox virus

Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of thecoding regions of all eight gene segments (Reconstructed1918 Influenza virus)

Ricin
Rickettsia prowazekii
SARS-associated coronavirus (SARS-CoV)
Saxitoxin

South American Haemorrhagic Fever viruses:
- Chapare
- Guanarito
- Junin
- Machupo
- Sabia

Staphylococcal enterotoxins A,B,C,D,E subtypes
T-2 toxin
Tetrodotoxin

Tick-borne encephalitis complex (flavi) viruses:
- Far Eastern subtype
- Siberian subtype

Kyasanur Forest disease virus
Omsk hemorrhagic fever virus
Variola major virus (Smallpox virus)
Variola minor virus (Alastrim)
Yersinia pestis

Bacillus anthracis
Bacillus anthracis Pasteur strain
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei
Burkholderia pseudomallei
Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan equine encephalitis virus
African horse sickness virus
African swine fever virus
Avian influenza virus
Classical swine fever virus
Foot-and-mouth disease virus
Goat pox virus
Lumpy skin disease virus
Mycoplasma capricolum
Mycoplasma mycoides
Newcastle disease virus
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Peronosclerospora philippinensis (Peronosclerosporasacchari)
Phoma glycinicola (formerly Pyrenochaeta glycines)
Ralstonia solanacearum
Rathayibacter toxicus
Sclerophthora rayssiae
Synchytrium endobioticum
Xanthomonas oryzae

What To Do If You Encounter A Select Agent

What is a Select Agent or Toxin?

Select agents and toxins are biological agents and toxins that could pose a severe threat to public health, animal and plant health, or to animal or plant products. The U.S. list of Select Agents and Toxins is maintained by the Centers for Disease Control and Prevention (CDC) and the Animal and Plant Health Inspection Service (APHIS), and are found in the select agent regulations (42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331).

What to do?

- Immediately contain the select or toxin in a location to ensure the safety and security of the material.
- Immediately contact the Federal Select Agent Program to report the findings and wait for further instructions.

  Animal and Plant Health Inspection Service
  Agriculture Select Agent Services
  Email: AgSAS@aphis.usda.gov
  Phone: 301-851-3300 (option 3) (Normal business hours Mon - Fri)

  Centers for Disease Control and Prevention
  Division of Select Agents and Toxins
  Email: lrsat@cdc.gov
  Phone: 404-718-2000 (Normal business hours Mon - Fri)

- Secure the location where the material was discovered until such a time as it can be reviewed by safety and law enforcement personnel. If any suspicious activity is observed that may pose a risk to the security of the facility, its personnel, or the select agents or toxins, please immediately notify the FBI Weapons of Mass Destruction Coordinator. For information on the coordinator please call (202) 323-3300 or visit http://www.fbi.gov/contact-us/field.

- After material has been tested and a select agent or toxin identified, the institution should submit the APHIS/CDC Form 4, Report of the Identification of a Select Agent or Toxin within 7 calendar days to the Federal Select Agent Program.

For more information about the Federal Select Agent Program, go to www.selectagents.gov.

USDA

CDC

Tab B

IMPLEMENTATION OF RECOMMENDATIONS OF THE FEDERAL EXPERTS SECURITY ADVISORY PANEL (FESAP) AND THE FAST TRACK ACTION COMMITTEE ON SELECT AGENT REGULATIONS (FTAC-SAR)

October 2015

IMPLEMENTATION OF RECOMMENDATIONS OF THE FEDERAL EXPERTS SECURITY ADVISORY PANEL (FESAP) AND THE FAST TRACK ACTION COMMITTEE ON SELECT AGENT REGULATIONS (FTAC-SAR)

October 2015

RECOMMENDATION	IMPLEMENTATION PATHWAY AND PROJECTED TIMELINE	D/A LEAD(s)
Culture of Responsibility		
FESAP 1.1: Create and strengthen a culture that emphasizes biosafety, laboratory biosecurity, and responsible conduct in the life sciences. This culture of responsibility should be characterized by individual and institutional compliance with biosafety and laboratory biosecurity regulations, guidelines, standards, policies and procedures, and enhanced by effective training in biorisk management.	• Develop and incorporate bioethics modules and quality system training into laboratory biosafety and laboratory biosecurity training and/or research design. The training should include discussions of ethical and legal considerations, as well as the social relevance of life science research, and the range of dual-use concerns that arise due to the impact of science and technology on society, health, and national security. **[Action by July 2016]** • Promote bioethics and quality system training (creating and implementing quality planning and assurance, as well as quality control and quality improvement) that includes curricula on conduct that incorporates fundamental safety and security responsibilities expected of all life scientists. **[Action by September 2016]** • Develop semi-quantitative methods to evaluate the efficacy of training, education, codes of conduct, and similar interventions to reduce risk and improve safety in domestic research laboratories housing infectious agents and toxins. **[Action by December 2017]**	IBMWG IBMWG Study sponsored by HHS, USDA
Oversight		
FESAP 1.2: Require that all research institutions, in which human, plant, and/or animal infectious agents and toxins research is conducted, have an appropriate organizational and governance structure to ensure	• Develop an approach to require that all research institutions, in which human, plant, and/or animal infectious agents and toxins research is conducted, have an appropriate organizational and governance structure to ensure compliance	IBMWG

compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines.	with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines. Plan includes: – Approach external organizations including research and biosafety organizations in order to determine whether they have the relevant guidelines that they provide to their membership related to organizational and governance structures. – Compile all such policies and documents in a shared space for access and review for harmonization. **[Actions by March 30, 2016]**	
FESAP 1.3: Require that an appropriately constituted and qualified review entity validate local policies, laboratory protocols, and mitigation plans involving the inactivation, sterilization, or decontamination of biohazardous materials at research institutions.	• HHS and USDA will identify or constitute a review entity qualified to validate local policies, laboratory protocols, and mitigation plans involving the inactivation, sterilization, or decontamination of biohazardous materials at research institutions registered with the Federal Select Agent Program. **[Action by September 30, 2016]**	HHS, USDA
FTAC 11: Peer Advisory Mechanism: The FTAC recommends creating an expert panel or Federal Advisory Committee to serve as an external group that could share best practices or make recommendations to the Federal Select Agent Program (FSAP).	• Convene an interagency group to develop a mechanism for external stakeholders to engage with the FSAP to provide subject matter expertise, including development of recommendations on the specific role/mandate of the mechanism and its relationship with other mechanisms (e.g., FESAP, Interagency Select Agents and Toxins Advisory Committee [ISATTAC]). – Identify pros, cons, and feasibility of options. **[Action by December 2015]**	HHS and USDA lead with participation from FBI, DOI, DOD, DHS, EPA, DOC, and DOS

	– Obtain feedback from stakeholders and identify preferred option. **[Action by January 2016]** – Develop a plan to institute preferred option. **[Action by March 2016]** – Implement measures to establish preferred option. **[Action by June 2016]**	
Outreach and Education		
FESAP 1.4: Support the development and implementation of security awareness education programs/curriculum that: • **Underscore personal responsibility for safeguarding potentially hazardous biological agents;** • **Share information about security breaches that have occurred involving infectious or toxic materials;** • **Emphasize the need for self and peer reporting;** • **Discuss material protection strategies; and** • **Explain exploitation of life sciences research.**	• FBI has developed a security awareness program that is consistent with the recommendation and will work with interagency partners to assist with implementation - or in developing a program tailored for their use. **[Action by November 30, 2016]**. – **FBI recommends inclusion of an additional element:** Incorporate security awareness education as a means to reinforce existing safety, ethics, and other training programs and provide better understanding as to the rationale for the existence of compliance requirements associated with the Select Agent Program**.**	FBI
FESAP 1.5: Develop and implement strategies to ensure effective communication and awareness of biosafety, biocontainment, and biosecurity.	• Develop a strategic communications plan for biosafety, biocontainment, and biosecurity outreach and education. **[Action by January 2016]** • Support an outreach program to promote effective communication and awareness of biosafety, biocontainment, and laboratory biosecurity; improve biorisk	IBMWG

	management; and help coordinate interagency outreach activities that deal with biosafety, biocontainment, and laboratory biosecurity. **[Action to be ongoing]**	
FTAC 2: Public Release of information: The FTAC recommends that information about biological select agents and toxins (BSAT) research, including laboratory incidents, be periodically provided to the public, and that Federal BSAT laboratories adopt, to the maximum extent feasible, a policy of transparency regarding both the agents used and laboratory incidents.	• FSAP will release aggregate information on laboratory incidents on an annual basis. **[Action to be conducted annually beginning in June 2016]** • Federal BSAT laboratories develop and adopt a policy of transparency, to the maximum extent feasible, regarding both the agents used and laboratory incidents. **[Action to be ongoing]** • Encourage non-Federal BSAT laboratories to adopt a policy of transparency, to the maximum extent feasible and based on federal guidance, regarding both the agents used and laboratory incidents. **[Action to be ongoing]**	FSAP Federal D/As with BSAT laboratories Federal D/As with BSAT laboratories
FTAC 3: Sharing Best Practices: The FTAC recommends members of the regulated community establish a mechanism for sharing best practices.	• Consult with relevant stakeholders to identify a mechanism for sharing best practices; and, support establishment of a plan to implement. **[Action by January 2016]**	HHS/CDC and USDA/ARS in collaboration with stakeholders
FTAC 12: International Engagement: The FTAC recommends international engagement to explore harmonization of pathogen security standards and ensure understanding of the rationale for, and implementation of, the SAR-equivalent standards by collaborating foreign governments.	• Support efforts, including convening and expanding membership of the International Expert Group for Biosafety and Biosecurity Regulation (IEGBBR), an informal ad hoc group consisting of members from several countries for the purpose of sharing the experiences by individuals responsible for development and implementation of biosafety and security regulations governing the possession, importation and use of infectious disease agents and toxins by biological laboratories in accordance with the Biological and Toxin Weapons Convention and the United Nations	FSAP

	Security Council Resolution 1540. **[Action by June 2016]** • Initiate one or more international meetings to discuss pathogen security regulations, policies, and practices, and opportunities to strengthen biorisk management on an international basis. **[Action by August 2017]**	DOS and/or DOD with FSAP and other D/A support
Applied Biosafety Research		
FESAP 1.6: Develop and maintain a robust federally-supported program of applied biosafety research to create additional evidence-based practices and technologies, and to update existing practices and operations.	• HHS, USDA, DOD, and DHS to convene a small group to develop an implementation plan, timeline, and resource strategy including potential for consultation with external stakeholders**. [Action by January 30, 2016]** Elements of plan include: – Determine whether any entities maintain an existing database on applied biosafety research. – Support study to develop a national research agenda for applied biosafety with a one health focus to improve the management of biohazard risks. – Develop a sustainable program of applied biosafety research to create additional and update existing evidence based practices and technologies for the laboratory and the field. – Maintain applied biosafety research program.	Lead: HHS, USDA; with support from DHS, DOD
Incident Reporting		
FESAP 1.7: Establish a new voluntary, anonymous, non-	• Pilot Incident Reporting System on HHS intranet. **[Action by**	HHS, IBMWG

punitive incident-reporting system for research laboratories that would ensure the protection of sensitive and private information, as necessary.	**December 2016]** • Pilot incident reporting system by other Federal D/A, dependent on outcome of pilot. **[Action by December 2017]** • Expand incident reporting system to non-Federal stakeholders, dependent on outcome of pilot. **[Action by December 2018]**	Other Federal D/As Federal D/As
Material Accountability		
FESAP 1.8: Increase awareness of existing material accountability best practices, and support the establishment of material accountability procedures where none currently exist. **and** **FESAP 2.5: Improve guidance regarding working stocks and inventory control.**	• Establish a small group of subject matter experts and implement next steps to enhance inventory control, including mechanisms to ensure biological material ownership and responsibility is transferred when an individual leaves the organization. Plan includes: – Approach external groups for best practices on pathogen inventory. – Develop a best practice guidance for the research community. – Ask all research entities to develop and adopt a specimen management policy. – Require all D/A to incorporate a select agent annex or other specificity into their scientific collections policies that ensure accountability. – Improve guidance regarding inventory control for working stocks.	HHS, USDA, DHS, and DOD

	[Actions above by January 30, 2016] - Develop a strategic communication plan to address BSAT material accountability **[Action by March 2016]** - Support outreach efforts to stakeholders (federal and non-federal) to address BSAT material accountability. **[Action to be ongoing]**	IBMWG IBMWG
FTAC 6: Inventory Control Requirements: The FTAC recommends retaining requirements to maintain inventories of samples containing biological select agents and toxins, while ensuring that BSAT institutions are not requested to characterize biological agents quantitatively.	• Review, and update if necessary, guidance and training related to inventory management to specifically preclude the quantitative characterization of biological agents (e.g., Guidance on the Inventory of Select Agents and Toxins 7 CFR Part 331, 9 CFR Part 121, 42 CFR Part 73; 16 April 2015). **[Action by January 2016]**	FSAP
Inspection Processes		
FTAC 7: Consistency of Inspections: The FTAC recommends development of an approach to improve the consistency of the inspection process across inspectors, inspecting agencies, and inspected sites.	• Establish an interagency working group to develop a mechanism to solicit input from stakeholders related to inconsistencies and other issues experienced by stakeholders during inspections. Solicit concrete examples of inspection inconsistencies and issues. **[Action by January 2016]** • The FSAP will gather concrete examples of the inconsistencies and issues identified by stakeholders, and develop an approach to improving the consistency of inspections and resolving these issues. **[Action by October 2016]**	FSAP FSAP
FTAC 8: Improve Customer Service in Communicating with Regulated Entities: The FTAC recommends improving	• Develop policies and practices to communicate inspection reports to registered entities within 60 days of the completion of the	FSAP

communication before and after site inspections and improving the timeliness of inspection reports.	inspection. **[Action to be ongoing]** • Explore the feasibility of the establishment of an electronic mechanism for communication of information between the registered entities and the FSAP related to inspections and identify elements of the mechanism. **[Action by June 2016]** • If feasible, make progress toward establishment of an electronic mechanism (e.g., Electronic National Select Agent Registry [E-NSAR]) for communication of information between the registered entities and the FSAP related to inspections. **[Action by September 2016]**	FSAP FSAP
FTAC 9: Categorize Inspection Findings: The FTAC recommends developing a system to categorize findings on inspection reports.	• Develop definitions for categories of findings on inspection reports (e.g., administrative, important, critical). **[Action by February 2016]**	FSAP
FTAC 10: Appeals Process: The FTAC recommends expanding the appeals process for institutions to adjudicate disputed findings in inspection reports.	• Develop a formal mechanism for entities to appeal inspection findings which are disputed by an entity. [**Action by February 2016]**	FSAP
Regulations and Guidelines		
FESAP 2.1: Add a specific requirement for the documentation of the drills and exercises required in sections 11 (Security), 12 (Biosafety), and 14 (Incident Response) of the current SAR.	• The Federal Select Agent Program is incorporating this regulatory change in the biennial review Notice of Proposed Rule. In practice, many registered entities already conduct this activity but the regulation change will ensure this occurs with all registered entities**. [Proposed publication in Summer 2016]**	FSAP
FESAP 2.2: Add a specific requirement to section 15 (Training) to include how a trainee can access the U.S.	• The Federal Select Agent Program is incorporating this regulatory change in the biennial review Notice of Proposed	FSAP

Department of Health and Human Services (HHS) and U.S. Department of Agriculture (USDA) Office of the Inspector General (OIG) Hotline to anonymously report a safety or security concern.	Rule**. [Proposed publication in Summer 2016]**	
FESAP 2.3: Optimize guidance to address integration of the Responsible Official (RO) with entity's biosafety and biosecurity oversight committee(s).	• The Federal Select Agent Program will incorporate this guidance into the Responsible Official Resource Manual. **[Target completion by November 2015]**	FSAP
FESAP 2.4: Modify guidance documents to recommend that the composition of the local oversight committee(s) represent the breadth of stakeholders involved in developing and implementing institutional biosafety and biocontainment programs.	• Convene interagency group to review the requirements for various oversight committees in institutions that work with BSAT and recommend modification of these guidelines to: – Ensure that committee membership includes appropriate expertise and represents the breadth of stakeholders responsible for the execution of the biosafety and biocontainment programs at an institution, with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* as a model. – Ensure that effective communication and coordination exists between these institutional committees, so that the biocontainment labs have uniform and effective oversight. – Consider incorporating community engagement. **[Action by November 30, 2015]**	Lead: HHS; with support from DOD, USDA, DHS
FESAP 2.5: Improve guidance regarding working stocks and inventory control.	*See Material Accountability section*	

FESAP 2.6: Improve guidance for biosafety plans	• The Federal Select Agent Program has developed a template for biosafety plans and will move forward to develop guidance for creation of biosafety plans. In addition, the biosafety section of the select agent regulations will be expanded to specify required components of biosafety plans for registered entities. Target completion date of the guidance March 2016. **[Target publication of proposed rule in Summer 2016]**	FSAP
FESAP 2.7: Amend guidance documents to suggest that entities consider establishing policies on maximum work hours for high containment workers.	• The Federal Select Agent Program will incorporate this recommendation into its guidance for biosafety plans, which is under development. **[Target completion of the biosafety plan guidance is March 2016]** • HHS to coordinate with USDA, DOD, DHS and other D/A to determine next steps to update the *Biosafety in Microbiological and Biomedical Laboratories*. **[Action by April 2016]**	FSAP Lead: HHS with USDA, DOD, DHS, and other D/A
FESAP 2.8: Support U.S. Occupational Safety and Health Administration (OSHA) Infectious Diseases (ID) Standard.	• Discuss and identify awareness-raising activities and needs related to OSHA's proposed and final ID rules. **[Action by January 2016]** • Discuss development of an interagency listserv on infectious disease topics relevant to the ID Rulemaking and discuss a list of potential members to invite to join this ID listserv. **[Action by January 2016]** • If recommended by the IBMWG, develop a strategic communications and outreach plan. **[Action by July 2016]**	IBMWG

	• If recommended by the IBMWG, develop outreach materials (e.g., Frequently Asked Questions, fact sheet, etc.). **[Action by November 2016]** • Promote stakeholder awareness related to the publication of the proposed rule related to the OSHA ID standard. **[Action by December 2015]** • Promote stakeholder awareness related to the publication of the OSHA ID standard final rule. **[Action anticipated by December 2018]**	
FTAC 1: Regulation Interpretations: The FTAC recommends developing a formal mechanism for issuing, publicizing, and accepting requests for interpretations of the Select Agent Regulations (SAR).	• Consider development of a formal mechanism for accepting and responding to requests related to interpretations of the select agent regulations (SAR). **[Action by January 2016]** • Implement formal mechanism, if supported, for accepting and responding to requests related to interpretations of the SAR. **[Action by June 2016]** • FSAP will publish interpretations of the SAR based on requests, as is necessary and appropriate. **[Action to be ongoing]**	FSAP FSAP FSAP
FTAC 4: Individual-based Security Risk Assessments: The FTAC recommends that in the absence of specific information indicating otherwise, individuals who have been granted access to select agents or toxins at one BSAT institution be able to move to another BSAT institution without having to wait for a new Security Risk Assessment.	• Convene a working group to examine the desirability and feasibility of transferring the Security Risk Assessment or SRA determination from one entity to another entity in the absence of disqualifying information and to craft language for Notice of Proposed Rulemaking. **[Action by September 2016]** • If desirable and determined to be feasible, the FSAP will publish Notice of Proposed Rulemaking (NPRM) that proposes specific change to the regulations.	Lead: FBI; with support from and HHS, USDA FSAP

FTAC 5: Emergency Situations: The FTAC recommends development of a mechanism to expedite approvals or to relax Federal Select Agent Program (FSAP) requirements in response to time-urgent emergency situations.	• Convene a working group to examine the need for additional exemption processes in emergency situations. **[Action by November 2016]** • Determine what statutory adjustments may be needed to provide more flexibility in the emergency exemptions. **[Action by January 2016]**	FSAP FSAP
FTAC 13: Guidance for Customs Inspectors: The FTAC recommends providing better training and guidance for customs inspectors who process BSAT shipments.	• Develop guidance targeted for customs inspectors related to the select agent regulations. **[Action by January 2016]** • Train customs inspectors. **[Action to be ongoing]**	DHS , FSAP DHS
FESAP: The approach recommended is a three phase process characterized by Federal assessment (Phase I), external review (Phase II), and consideration of the recommendations of the external non-Federal review by the U.S. Government (USG) (Phase III). The proposed three-phase process will include the development of a 'best practices checklist' for departments and agencies to follow when they are considering the need to modify existing high and maximum containment laboratory space capacity.	• The IPC endorsed the approach recommended by the FESAP to determine the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT. The IPC approved implementation for all three phases of the recommended approach, including an external review that involves public stakeholders. The IPC discussed next steps to develop criteria for a review, which will take into account preparedness, safety, security, and research needs, as well as the U.S. international posture on this issue. – The FESAP will determine timeline to begin Phase One. [**Action by October 1, 2015]** – HHS, USDA, and DHS, in conjunction with OSTP and NSC staff, will convene a working group to oversee next steps	 FESAP HHS, USDA, DHS, OSTP, NSC

	and schedule first meeting. **[Action by October 1, 2015]** – State/ISN will factor in best practices from the U.S. policy, "Guiding Principles and Assessment Process Related to the Provision of Biocontainment Facilities to Foreign Countries."	State/ISN

LEGEND:

ARS	Agricultural Research Service
BSAT	Biological Select Agents and Toxins
CDC	Centers for Disease Control and Prevention
D/A	Department and Agency (federal)
DHS	Department of Homeland Security
DOC	Department of Commerce
DOD	Department of Defense
DOI	Department of Interior
DOS	Department of State
E-NSAR	Electronic National Select Agent Registry
EPA	Environmental Protection Agency
FBI	Federal Bureau of Investigation
FESAP	Federal Experts Security Advisory Panel
FSAP	Federal Select Agent Program
HHS	Department of Health and Human Services
IBMWG	Interagency Biorisk Management Working Group
ID	Infectious Diseases
IPC	Interagency Policy Committee
ISN	Bureau of International Security and Nonproliferation (ISN)
ISATTAC	Interagency Select Agents and Toxins Advisory Committee
NPRM	Notice of Proposed Rulemaking
NSC	National Security Council
OSHA	Occupational Safety and Health Administration
OSTP	Office of Science and Technology Policy (White House)
RO	Responsible Official

SAR	Select agent regulations
USDA	U.S. Department of Agriculture

Tab C

Report of the Federal Experts Security Advisory Panel

December 2014

Report of the Federal Experts Security Advisory Panel

Table of Contents

Report of the Federal Experts Security Advisory Panel

EXECUTIVE SUMMARY

On July 2, 2010, President Obama signed Executive Order 13546 "Optimizing the Security of Biological Select Agents and Toxins," which created and tasked the Federal Experts Security Advisory Panel (FESAP) to address policy issues relevant to the security of biological select agents and toxins (BSAT).

The FESAP successfully completed the tasks enumerated by Executive Order 13546 (see Appendix A), and was re-chartered to evaluate approaches to enhance biosafety and biosecurity in the United States (per Paper Interagency Policy Committee on Implementation of Executive Order 13546 decision memo dated July 18, 2014, from Laura Holgate, Senior Director, Weapons of Mass Destruction (WMD) Terrorism and Threat Reduction, National Security Council).

Recent incidents involving BSAT have raised serious safety and security policy issues. The White House National Security Council (NSC) staff tasked the FESAP, in September 2014, to 1) identify needs and gaps and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT; 2) identify actions and any regulatory changes to improve biosafety and biosecurity; and 3) identify an approach to determine the appropriate number of high-containment U.S. laboratories required to possess, use, or transfer BSAT. The NSC requested that the FESAP provide recommended actions to the Assistant to the President for Homeland Security and Counterterrorism, and the Assistant to the President for Science and Technology within 90 days of receiving the tasking.

In general, the FESAP concludes that the U.S. Government has developed a robust set of rules, regulations, and practices to inform safe, secure and responsible work and research with infectious agents and toxins that produce illness, death, and economic impact to the United States and cause global concerns. However, there are several improvements that may further mitigate the inherent risks in such work. A summary of the FESAP's recommended actions to address the FESAP's September 2014 charge follows.

Identification of Needs and Gaps, and Recommendations to Optimize Biosafety, Biosecurity, Oversight, and Inventory Management and Control for BSAT

The FESAP identified needs and gaps, and made recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT.

The recommendations are as follows:

- **Recommendation 1.1:** Create and strengthen a culture that emphasizes biosafety, laboratory biosecurity, and responsible conduct in the life sciences. This culture of responsibility should be characterized by individual and institutional compliance with biosafety and laboratory biosecurity regulations, guidelines, standards, policies and procedures, and enhanced by effective training in biorisk management.

- **Recommendation 1.2:** Require that all research institutions in which human, plant, and/or animal infectious agents and toxins research is conducted have an appropriate organizational and governance structure to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines.

- **Recommendation 1.3:** Require that an appropriately constituted and qualified review entity validate local policies, laboratory protocols, and mitigation plans involving the inactivation, sterilization, or decontamination of biohazardous materials at research institutions.

- **Recommendation 1.4:** Support the development and implementation of security awareness education programs/curriculum that:
    - Underscore personal responsibility for safeguarding potentially hazardous biological agents;
    - Share information about security breaches that have occurred involving infectious or toxic materials;
    - Emphasize the need for self and peer reporting;
    - Discuss material protection strategies; and
    - Explain exploitation of life sciences research.

- **Recommendation 1.5:** Develop and implement strategies to ensure effective communication and awareness of biosafety and biocontainment.

- **Recommendation 1.6:** Develop and maintain a robust federally-supported program of applied biosafety research to create additional evidence-based practices and technologies, and to update existing practices and operations.

- **Recommendation 1.7:** Establish a new voluntary, anonymous, non-punitive incident-reporting system for research laboratories that would ensure the protection of sensitive and private information, as necessary.

- **Recommendation 1.8:** Increase awareness of existing material accountability best practices, and support the establishment of material accountability procedures where none currently exist.

Identification of Actions and any Regulatory Changes to Improve Biosafety and Biosecurity

The FESAP identified actions and regulatory changes to improve biosafety and biosecurity.

Specific changes recommended by FESAP for the select agent regulations (SAR) follow:

- **Recommendation 2.1:** Add a specific requirement for the documentation of the drills and exercises required in sections 11 (Security), 12 (Biosafety), and 14 (Incident Response) of the current SAR.

- **Recommendation 2.2:** Add a specific requirement to section 15 (Training) to include how a trainee can access the U.S. Department of Health and Human Services (HHS) Office of the Inspector General (OIG) Hotline to anonymously report a safety or security concern.

Proposed enhancements to Select Agent Regulatory Guidance follow:

- **Recommendation 2.3:** Optimize guidance to address integration of the Responsible Official (RO) with entity's biosafety and biosecurity oversight committee(s).

- **Recommendation 2.4:** Modify guidance documents to recommend that the composition of the local oversight committee(s) represent the breadth of stakeholders involved in developing and implementing institutional biosafety and biocontainment programs.

- **Recommendation 2.5:** Improve guidance regarding working stocks and inventory control.

- **Recommendation 2.6:** Improve guidance for biosafety plans.

- **Recommendation 2.7:** Amend guidance documents to suggest that entities consider establishing policies on maximum work hours for high containment workers.

The FESAP supported another proposed regulatory tool for expanded federal oversight beyond BSAT:

- **Recommendation 2.8:** Support U.S. Occupational Safety and Health Administration (OSHA) Infectious Diseases Standard.

Identification of an Approach to Determine the Appropriate Number of High Containment U.S. Laboratories Required to Possess, Use, or Transfer BSAT

Federal departments and agencies must continually evaluate how to align their missions to protect human, animal and plant health against a constantly changing landscape of emerging diseases and novel opportunities as technology advances. These changes may require re-evaluation of biocontainment laboratory space needs within or across departments and agencies to remain current and viable.

The FESAP recommended an approach to determine the appropriate number of federally funded high containment U.S. laboratories required to possess, use, or transfer BSAT. The approach recommended is a three phase process characterized by federal assessment (Phase I), external non-federal review (Phase II), and consideration of the recommendations of the external non-federal review by the U.S. Government (USG) (Phase III). The proposed three phase process will include the development of a general USG 'best practices checklist' for departments and agencies to follow when they are considering the need to modify existing high and maximum containment laboratory space capacity.

Phase I: Federal Assessment

Phase I includes an internal federal review of the capacity needs for high containment space, and of the process that is used to address capacity needs. This review is comprised of two steps—1) the federal departments or agencies conduct an independent assessment of their need for high containment space based on mission requirements and in alignment with their strategic plans, and identify the steps they would use to address these needs, and 2) a review by a federal interagency panel of the need for high containment space based on national needs, and of the processes by which agencies meet those needs. The outcome will be a 'best practices checklist' that will be used as a guideline by departments and agencies when considering the construction of high or maximum containment laboratories. The best practices checklist will ensure that departments and agencies have considered the many different potential options to address their containment research needs and could potentially enable a reduction in the time and cost for planning; design; the release of the request for funding; the award; and the construction of high and maximum containment laboratories.

Step 1 of Phase I is addressed independently by federal departments or agencies. Step 2 of Phase I involves a federal interagency review panel. The federal interagency review panel should be carefully chosen to ensure the least possible conflict of interest for participants and the most objective expert review possible, while retaining the ability to draw on relevant technical experts in the respective departments and agencies. The federal interagency review panel can provide general direction and guidance to the departments and agencies, but should not be involved in formal approval of specific department and agency plans to add to or reduce high containment laboratory space.

Department and Agency Independent Aassessment of Current and Projected Space Needs

Step 1: **Individual departments and agencies will independently examine the use and availability of high containment laboratory space, including the process they use to acquire the necessary containment laboratory space. Departments and agencies will address how they meet mission requirements in relationship to their strategic plans with the goal of preparing an overall assessment of available space to meet current and projected needs.**

Individual departments and agencies will:

- Examine their mission in the context of high containment space to ensure it can meet mission requirements.
- Articulate information about methodology used to assess current and projected space use.
- Articulate assumptions made in projecting future space requirements.
- Provide information about the adequacy of current space and available space to meet current and projected needs.
- Identify any concerns related to use of available space.
- Identify gaps in the use of available space.
- Identify "best practices" for a checklist that could be generally used by other departments and agencies to streamline the process of planning and designing containment space.
- Provide an overall assessment of current and projected needs to meet their mission requirements.

Federal Review Panel Assessment

Step 2: **Federal interagency review panel will examine department and agency assessments in totality.**

The federal interagency review panel will:

- Review the planning assumptions with respect to future laboratory space requirements and achieve consensus, where possible, on any assumptions that would relate to more than one department or agency's plans.
- Provide an overall assessment of department and agency assessments to meet current and projected national needs.
- Identify overall projected high containment space needs and/or opportunities for more effective use of existing space and optimization of efficiencies, where possible.
- Provide strategic advice related to alignment of current and projected department and agency high containment laboratory capacity needs with national needs.
- Develop generalizable principles, standardized methodologies, and templates (e.g., "best practices" checklist) that could be applied to guide assessments of current and projected needs for high containment space, as well as mechanisms to efficiently meet those needs.
- Develop criteria and design a mechanism for external stakeholder review and analyze.

Phase II: External Review Panel Assessment

***Step 3*: Establish an external non-federal entity to examine the outcome of Phase I in the context of national needs.**

The Phase II review, conducted under criteria developed in Phase I, provides the opportunity for review of USG plans from a perspective broader than that of any single agency. This review can consider factors such as aggregate national need and can provide perspective on potential efficiencies resulting from collaborative work that agencies might not have identified. It also provides the opportunity to consider factors relating to the optimal amount of national biocontainment space that individual agency assessments may not have considered. The step provides a mechanism for an objective assessment of laboratory use and needs and would help to enable further transparency and public trust and confidence related to the number of high containment laboratories.

The external non-federal entity will:

- Validate (or make suggestions for revision of) overall needs and gaps in high containment space in meeting current capacity needs.
- Validate (or make suggestions for revision of) overall projected high containment space needs.
- Provide an overall assessment of the federal review panel's overall assessment to meet current and projected national needs.
- Provide strategic advice related to current and projected high containment needs to meet national needs.
- Identify factors relating to the optimal amount of national biocontainment space that individual agency assessments may not have considered or that may fall outside the purview of the Executive Branch.

- Identify potential efficiencies that could result from collaborative work that agencies may not have identified.
- Validate (or make suggestions for revision of) generalizable principles that can be applied to guide assessments of the current and projected need for high containment space, as well as mechanisms to efficiently meet those needs.

Phase III: USG Consideration of External Review Panel Assessment

***Step 4*: The USG will carefully consider the assessment resulting from Phase II to ensure any recommendations are practical, implementable and appropriately incorporated into agency planning processes.**

Recommendations resulting from Phase II of this process will be examined by an internal federal government group to ensure high containment space considerations have been addressed by federal department and agency processes. Recommendations may include actions external to a single federal department or agency.

The USG will:

- Consider the assessment developed by the non-federal entity to ensure any recommendations are practical and can be implemented.
- Encourage implementation of recommendations in a consistent approach by various federal departments and agencies.
- Develop a central clearinghouse or a mechanism to collect best practices for considerations related to proceeding to design and build once decision is made.
- Provide general direction and guidance to departments and agencies considering modifying high containment laboratory capacity - without assuming a formal approval of specific department and agency high containment laboratory space decisions.
- Develop a standardized mechanism, at the whole-of-government level, to formally acknowledge the accession of new space.

Report of the Federal Experts Security Advisory Panel

I. FEDERAL EXPERTS SECURITY ADVISORY PANEL OVERVIEW AND CHARGE TO THE PANEL

On July 2, 2010, President Obama signed Executive Order 13546 "Optimizing the Security of Biological Select Agents and Toxins," which created and tasked the FESAP with addressing policy issues relevant to the security of BSAT. (For definitions of terms used in this report, see the Glossary.)

The FESAP successfully completed the tasks enumerated by Executive Order 13546 (see Appendix A) and was re-chartered to evaluate approaches to enhance biosafety and biosecurity in the United States (per Paper Interagency Policy Committee on Implementation of Executive Order 13546 decision memo dated July 18, 2014, from Laura Holgate, Senior Director, WMD Terrorism and Threat Reduction, NSC).

Recent incidents involving BSAT have raised serious safety and security policy issues. Specifically, within several weeks, there was a discovery in a federal facility of smallpox samples in a decades old collection of biological materials that had been unknowingly not inventoried; there was a breach of safety using a unvalidated procedure to inactivate anthrax spores for use at a lower biocontainment level; and finally there was a cross-contamination of avian influenza specimens in which a strain with higher avian pathogenicity was accidently introduced into experimental samples of a lower pathogenicity strain. None of these events resulted in human illness, but suggested that lapses in adherence to accepted methods and protocols had occurred. The NSC sought to understand the root cause for these events and whether there were sufficient regulations, processes, and oversight in the current U.S. framework for biorisk[1] management that should have mitigated or prevented these events. The White House NSC staff tasked the FESAP, in September 2014, to 1) identify needs and gaps and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT; 2) identify actions and any regulatory changes to improve biosafety and biosecurity; and 3) identify an approach to determine the appropriate number of high-containment U.S. laboratories required to possess, use, or transfer BSAT. The NSC

[1] "Biorisk" is the combination of the probability of the occurrence of harm and the severity of that harm where the sour**ce** of harm is a biological agent or toxin (adapted from ISO/IEC Guide 51:1999). "Biorisk management" is the effective management of risks posed by working with hazardous biological agents in laboratories; it includes a range of practices and procedures to ensure the biosecurity, biosafety, and biocontainment of high-consequence pathogens.

requested that the FESAP provide recommended actions to the Assistant to the President for Homeland Security and Counterterrorism, and the Assistant to the President for Science and Technology within 90 days of receiving the tasking.

To generate this report, the FESAP reviewed the current system of biosafety, biocontainment, and biosecurity oversight, and where appropriate, built on recommendations from previous reports relevant to the tasks outlined above that have been made by and for the Federal Government on biosafety and biosecurity. The FESAP considered the work of other entities to include relevant recommendations from the Interagency Biorisk Management Working Group, the Working Group on Strengthening the Biosecurity of the United States, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight, the Working Group on Strengthening the Biosecurity of the United States of the United States, and the Government Accountability Office. The FESAP also reviewed corrective actions identified as a result of a Federal Government-wide Safety Stand-Down[2] in 2014 and the after-action assessments from the three recent U.S. biosafety and biosecurity incidents.

To accomplish the goals listed above, the FESAP utilized appropriate federal subject matter experts (SMEs) from its members' departments and agencies to populate three working groups, and each working group focused on one of the three taskings noted above. The FESAP's process of deliberation and consultation also included soliciting perspectives and input from key stakeholders, including the American Biological Safety Association (ABSA) and the American Society for Microbiology (ASM).

[2] On August 19, 2014, the White House NSC and OSTP sent a joint memo to all federal departments and agencies involved in life-sciences research urging them to take immediate and longer-term steps aimed at addressing the underlying causes of the recent laboratory incidents and strengthening overall biosafety and biosecurity at federal facilities. All relevant federal facilities—including extramural facilities that receive federal funding—were urged to conduct a "Safety Stand-Down" in the near-term, during which senior leaders would review laboratory biosafety and biosecurity best practices and protocols, and would develop and implement plans for sustained inventory monitoring. The August 19, 2014 memo also tasked the National Science and Technology Council will establish an interagency group to conduct a comprehensive review of the impact that the SAR have had on science, technology, and national security. The memo is available at https://www.whitehouse.gov/sites/default/files/microsites/ostp/enhancing_biosafety_and_biosecurity_19aug2014_final.pdf.

The White House NSC and the Office of Science and Technology Policy (OSTP) staffs will review the FESAP recommendations and task departments and agencies, as appropriate, with developing implementation plans.

Mission

The mission of the FESAP is to make technical and substantive recommendations concerning the appropriate safeguards and security standards for persons possessing, using, or transferring BSAT. The recommendations shall be commensurate with the risk that such agents or toxins pose to public health and safety, to animal and plant health, and to animal and plant products, including the risk of their use in domestic or international terrorism.

Function

The duties of the FESAP are solely advisory, and shall extend only to the submission of advice or recommendations. Advice and recommended actions developed by the FESAP for this report are provided to the Assistant to the President for Homeland Security and Counterterrorism and the Assistant to the President for Science and Technology.

Membership of the FESAP

The FESAP is co-chaired by HHS and U.S. Department of Agriculture (USDA), and is comprised of representatives from a broad range of federal departments and agencies that have responsibility for and oversight of work with BSAT and other biological agents at research facilities. In addition to HHS and USDA, the members of the FESAP include representatives from the Departments of Commerce (DOC), Defense (DOD), Energy (DOE), Homeland Security (DHS), Justice (DOJ), Labor (DOL), State (DOS), Transportation (DOT), Veterans' Affairs (VA), as well as the Environmental Protection Agency (EPA), the National Science Foundation (NSF), National Security Council (NSC), Office of the Director of National Intelligence (ODNI), Office of Science and Technology Policy (OSTP), and the Joint Chiefs of Staff. See Appendix B for more information about the FESAP's membership.

For the purpose of developing recommended actions for this report, the FESAP convened three separate working groups, each co-chaired by senior managers among federal departments comprising the FESAP, and relied on the expertise of more than 140 federal experts among federal departments and offices.

II. IDENTIFICATION OF NEEDS AND GAPS, AND RECOMMENDATIONS TO OPTIMIZE BIOSAFETY, BIOSECURITY, OVERSIGHT, AND INVENTORY MANAGEMENT AND CONTROL FOR BSAT

Scientific research is crucial to the long term health security and wellness of the public, animals, plants, the environment, and our economy. The Administration is committed to fostering progress in the life sciences to include peaceful research involving BSAT, as well as non-BSAT, while at the same time ensuring that work is conducted in a safe and secure manner. The FESAP was tasked to identify needs, gaps, and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT.

BACKGROUND

Charge

To strengthen USG oversight for work with infectious agents and toxins, including (but not limited to) BSAT, the White House NSC requested that the FESAP undertake a comprehensive federal review and identify specific recommendations to strengthen the Government's biosafety and biosecurity practices and oversight system for federally-funded activities, consistent with the need to realize the public health and security benefits of such work. More specifically, with respect to federally-funded activities, the FESAP was asked to identify needs and gaps, and to provide recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT.

Scope

The scope of activities considered by the FESAP for this section of the report includes life science laboratory research activities in all sectors utilizing BSAT. However, the majority of the FESAP's recommendations have broader applicability to non-BSAT agents. Activities potentially involving BSAT that take place in diagnostic and treatment (non-research) facilities such as hospitals, clinics, veterinary, and food diagnostic laboratories were considered beyond the scope of this section of the report.

Approach

To generate the recommendations focused on optimizing biosafety, biosecurity, oversight, and inventory management control, the FESAP conducted a comprehensive assessment of the current biorisk management framework. The FESAP examined the current landscape of activities and efforts to strengthen biorisk management, leveraged recommendations made by other entities (e.g., Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight, Working Group on Strengthening Biosecurity of the United States, Interagency Biorisk Management Working Group, and Government Accountability reports), examined corrective actions identified as a result of the Safety Stand-Down and after-action assessments from the recent U.S. biosafety and biosecurity incidents, and reviewed the lessons learned from recent laboratory incidents.[3] The FESAP's process of deliberation and consultation also included soliciting perspectives and input from key stakeholders, specifically ABSA and ASM. During this process, the FESAP identified gaps and needs, and developed recommendations to address those gaps and needs.

IDENTIFICATION OF NEEDS AND GAPS, AND RECOMMENDATIONS TO OPTIMIZE BIOSAFETY, BIOSECURITY, OVERSIGHT, AND INVENTORY MANAGEMENT AND CONTROL FOR BSAT

The FESAP reviewed the current system of biosafety, biocontainment, and biosecurity oversight, and identified progress that has occurred toward addressing recommendations developed by other biosafety and biosecurity working groups.

The FESAP identified needs and gaps in biorisk management, and recognized that the biorisk management framework in the United States could be enhanced. The FESAP developed eight recommendations for implementation by the Federal Government to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT. Appendix C provides an overview of the needs and gaps related to biorisk management, as well as recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control. In this section of the report, each area for improvement is generally described together with specific issues, recommendations, and rationale for the recommendations of the FESAP. Recommendations were developed without consideration of potential competing priorities across the Federal Government,

[3] Some of the findings and recommendations based on the recent incidents are available at http://www.cdc.gov/about/lab-safety/.

and implementation of the recommendations would be subject to the availability of resources.

Biorisk Management (Biosafety and Biosecurity)

Effective biorisk management practices at individual laboratory facilities are critical components of a safe and effective research enterprise. The Federal Government is committed to the highest quality of design, construction, maintenance of biocontainment facilities, rigorous training of personnel who work in these laboratories, and the safe conduct of research and research-related activities that occur within these facilities. Effective biosafety and biosecurity programs are developed through ongoing biorisk assessments and implementation of effective countermeasures to reduce risk at the local, institutional, and laboratory level where research is conducted. Institutions that support microbiological and biomedical research have a fundamental responsibility to ensure that biological hazards are managed in a manner that effectively mitigates risk to to prevent unintended transmission to individuals, the community, or the environment. Risk management involves collaborative effort between scientific researchers, Federal Select Agent Program (FSAP) Responsible Officials (ROs), biosafety, and security professionals to identify safety and security hazards associated with biocontainment research activities, conduct appropriate assessments, and formulate appropriate mitigation measures to reduce risk. The central role of institutionally driven biorisk management is reflected in federal guidance documents that support performance-based approaches to implementing laboratory biosafety and biosecurity measures.

CULTURE OF BIOSAFETY, BIOSECURITY, AND RESPONSIBLE CONDUCT IN THE LIFE SCIENCES

Recent incidents involving BSAT have focused attention on the need to enhance and sustain the culture of biosafety, biosecurity, and responsible conduct in the life sciences. Incidents included the discovery of vials labeled "variola," the virus responsible for the disease smallpox, in a storage room in a Food and Drug Administration (FDA) laboratory located on the Bethesda campus of the National Institutes of Health (NIH); the potential exposure of staff members at the Centers for Disease Control and Prevention (CDC) to *Bacillus anthracis*; and the inadvertent cross-contamination of a low pathogenic avian influenza (LPAI) A (H9N2) virus sample with a highly pathogenic avian influenza (HPAI) A (H5N1) virus, and the subsequent shipment of the contaminated culture to an external high-containment laboratory. In each of these cases, compliance with existing regulations, policies and Standard Operating Procedures (SOPs) should have precluded these incidents from occurring, yet they still occurred.

Recommendation 1.1

- **Create and strengthen a culture that emphasizes biosafety, laboratory biosecurity, and responsible conduct in the life sciences. This culture of responsibility should be characterized by individual and institutional compliance with biosafety and laboratory biosecurity regulations, guidelines, standards, policies and procedures, and enhanced by effective training in biorisk management.**

In the report, *Safe Science: Promoting a Culture of Safety in Academic Chemical Research*, the National Research Council of the National Academies identified key features of an effective laboratory research safety culture.[4] Elements identified by the Committee as necessary to ensure a viable research safety culture include:

1. "Demonstration of safety as a core institutional value for the entire institution. This requires more than statements from leadership. It requires concrete demonstrations of how this value is prioritized and implemented throughout the organization.
2. Articulation of clear roles, responsibilities, authorities, and accountabilities for those directly involved in research safety within the laboratory, namely the faculty/principal investigator (PI), laboratory researchers, and the Environmental Health and Safety (EH&S) staff that support lab safety.
3. Support for a strong EH&S program that is able to provide the technical support and expertise necessary to maintain strong safety programs in research."[5]

The World Health Organization (WHO) guidance, *Responsible Life Science Research for Global Health Security,*[6] also emphasizes that a "culture of scientific integrity and excellence, distinguished by openness, honesty, accountability and responsibility…is the best protection against the possibility of accidents and deliberate misuse, and the best

[4] *Safe Science: Promoting a Culture of Safety in Academic Chemical Research* by the Committee on Establishing and Promoting a Culture of Safety in Academic Laboratory Research, Board on Chemical Sciences and Technology, Division on Earth and Life Studies, Board on Human-Systems Integration, Division of Behavioral and Social Sciences and Education, National Research Council of The National Academies is available at: http://dels.nas.edu/Report/Safe-Science-Promoting-Culture/18706.

[5] *Safe Science: Promoting a Culture of Safety in Academic Chemical Research* by the Committee on Establishing and Promoting a Culture of Safety in Academic Laboratory Research.

[6] WHO guidance, *Responsible Life Science Research for Global Health Security* is available at: http://whqlibdoc.who.int/hq/2010/WHO_HSE_GAR_BDP_2010.2_eng.pdf.

guarantee of scientific progress and development." The guidance also underscores that "A culture of responsible life sciences practice is most likely to result when the leadership within the organization supports and fosters such a management framework."

Senior institutional leadership efforts to establish biosafety and laboratory biosecurity as core values of the institution's vision for research with infectious agents and toxins is important for establishing and enhancing a culture of responsibility in the life sciences. Sufficient management infrastructure and staff empowered with the authority to ensure institutional compliance with all applicable laboratory biosafety and biosecurity policies and requirements contribute to a safe and secure environment to conduct life science research. Finally, the training of individual scientific researchers and research support staff, and rigorous adherence to institutional biorisk management policies are crucial to minimizing laboratory incidents in the area of biosafety and biosecurity.

Responsible conduct of life sciences research is characterized by full accountability and compliance with all applicable regulations, policies, and procedures at the local, institutional, and laboratory level. Heightened emphasis on biosafety, biosecurity, and responsible conduct in the life sciences enables individuals and/or institutions to respond effectively to familiar and unfamiliar biosafety challenges or security threats to materials and facilities—including insiders with malicious intent—out of carefully nurtured habit rather than by improvisation.

The recommendation to create, strengthen, and sustain a culture of biosafety, laboratory biosecurity, and responsible conduct in the life sciences requires adequate training of laboratory personnel on those critical safety behaviors to assure a level of competence that maximizes their own safety and that of the community. A robust and comprehensive concept of training and vigilance reinforces the framework of laws and regulations, and builds on individual and collective responsibility. Thus, the establishment and promotion of an expectation for learning and acquiring competencies coupled with the provision of formal training programs and resources is important.

At the federal level, a range of concrete actions can be taken to strengthen and sustain the culture of biosafety, biosecurity, and the responsible conduct of science:

- Promotion of bioethics training that includes curricula on conduct that incorporates fundamental safety and security responsibilities expected of all life scientists.
- Development and incorporation of bioethics modules into laboratory biosafety and laboratory biosecurity training and/or research design. The training should include discussions of ethical and legal considerations, as well as the social

relevance of life science research, and the range of dual-use conundrums and dilemmas that arise due to the impact of science and technology on society, health, and national security. Efforts should be undertaken to encourage institutional leadership to support and implement bioethics training within their institution's programs as a component of training.

- Development of semi-quantitative methods to evaluate the efficacy of training, education, codes of conduct, and similar interventions to reduce risk and improve safety in domestic research laboratories housing infectious agents and toxins.

Oversight

Effective oversight of BSAT is achieved through proper management programs at the institutional and laboratory levels where research is conducted, in combination with the oversight provided at the federal, state, tribal, and municipal level.

At the federal level, the current biorisk management oversight framework is comprised of regulations, guidelines, and policies. The SAR implement Title II, Subtitle A and Subtitle B (also known as the Agricultural Bioterrorism Protection Act of 2002) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and set forth the requirements for the possession, use, and transfer of select agents and toxins.[7] The FSAP Regulations are in the Code of Federal Regulations (CFR) as follows: 42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331.

The Export Administration Regulations (15 CFR 730-774), enforced by DOC, pertain to the export and re-export of commodities, software, and technology, including biological commodities.[8] The DOT (49 CFR 171-180, Transportation, 49 CFR 100-185, Hazardous Materials Regulations) establishes requirements for the safe transportation and shipment of infectious substances.[9]

The Bloodborne Pathogens Standard (29 CFR 1910.1030), enforced by the OSHA, details the infection controls required in the workplace to prevent worker exposure to blood and other potentially infectious materials.[10] More broadly, the General Duty Clause

[7] Information about the SAR is available at: www.selectagents.gov..
[8] The Export Administration Regulations **(15 CFR 730-774)** are available at: https://www.bis.doc.gov/index.php/regulations/export-administration-regulations-ear.
[9] The DOT regulations **d**etailing the requirements for transportation and shipment of infectious substances are available at: http://www.gpo.gov/fdsys/pkg/CFR-2010-title49-vol1/content-detail.html.
[10] The Bloodborne Pathogens Standard (29 CFR 1910.1030) is available at: http://www.gpo.gov/fdsys/pkg/CFR-2010-title29-vol6/xml/CFR-2010-title29-vol6-sec1910-1030.xml.

(Section (5)(a)(1)) of the Occupational Safety and Health Act (OSH Act) of 1970 (P. L.91-596; 84 STAT. 1590) applies to all workplaces, and states: "Each employer… shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees…"[11]

The *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*) is a manual published jointly by the NIH and CDC that describes the code of practice for biosafety and biocontainment in the United States. The fifth edition was published in 2007 and revised in December 2009.[12] The *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) specify scientifically-based practices for constructing and handling recombinant or synthetic nucleic acid molecules, and cells, organisms and viruses containing such molecules. The *NIH Guidelines* also articulate the responsibilities of institutions, investigators, and Institutional Biosafety Committees (IBCs) at institutions that receive any support for recombinant or synthetic nucleic acid research from the NIH.[13]

APPROPRIATE ORGANIZATIONAL AND GOVERNANCE STRUCTURE TO ENSURE COMPLIANCE WITH BIOSAFETY AND BIOCONTAINMENT REGULATIONS AND GUIDELINES

ASM and ABSA have recommended that institutions performing work with BSAT have a credentialed biosafety professional on staff. Some institutions have voluntarily adopted this recommendation, which demonstrates significant progress towards the establishment of a stronger biosafety oversight system. However, biosafety officers (BSOs)[14] are not always empowered with the level of authority required to implement critical changes that are needed to strengthen the institution's biorisk management program, which can impede efforts to introduce new practices and management strategies intended to enhance biosafety and biosecurity.

[11] The OSH Act of 1970 is available at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=3359&p_table=oshact.
[12] The *BMBL* is available at: http://www.cdc.gov/biosafety/publications/bmbl5/index.htm.
[13] The *NIH Guidelines For Research Involving Recombinant Or Synthetic Nucleic Acid Molecules (NIH Guidelines),* November 2013, is available at: http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.
[14] The role of a biosafety officer is described in the *NIH Guidelines* (See section IV-B-3.)

Protocol- and site-specific risk assessment and mitigation are critical components of a strong biorisk management program. A biosafety program, often with the support of an IBC, could be tasked with conducting biological risk assessments to evaluate protocols involving infectious agents and toxins, and assess potential hazards that may be involved. As a condition of funding, institutions that conduct research subject to the *NIH Guidelines* must establish an IBC for local oversight of these activities, including the review and approval of research involving recombinant or synthetic nucleic acid molecules. While the scope of authority for many IBCs has been voluntarily expanded to include oversight of research involving *non*-recombinant microorganisms, there is currently no requirement or consistent mechanism for the evaluation of safety concerns associated with this area of research.

Furthermore, institutions registered with the FSAP are required to designate a RO with the knowledge, skills, and authority needed to ensure institutional (entity) compliance with the SAR.

This creates a clear governance structure for BSAT compliance; however, there is no requirement to establish an equivalent system for institutional oversight of research involving non-BSAT agents to ensure uniform adherence to laboratory biosafety and biosecurity standards involving non-regulated infectious agents and toxins. Efforts to improve the quality of local biorisk management systems are significantly hampered without sufficient institutional authority, support, and programmatic and policy shifts necessary to clearly assign local responsibilities and expectations for the oversight of non-BSAT infectious materials or biological toxins.

Recommendation 1.2

- **Require that all research institutions in which human, plant, and/or animal infectious agents and toxins research is conducted have an appropriate organizational and governance structure to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines.**

An appropriate governance structure for the conduct of research would help ensure the institutional compliance framework includes effective strategies for the oversight of biosafety and biosecurity in research laboratories. Although local oversight systems vary between institutions, an appropriate governance structure should include specific elements necessary to empower institutional officials and laboratory workers to implement improvements in biosafety and biosecurity. An appropriate governance structure should include support for clear delegation of responsibility and authority for institutional biosafety officials.

Appointment of a qualified BSO, knowledgeable in the types of research conducted by the institution and with the ability to perform detailed hazard analysis, risk assessments, and to develop mitigation strategies related to research protocols, is an essential component of an enhanced governance structure and institutional oversight system. Both ABSA[15] and the National Registry for Certified Microbiologists (NRCM)[16] have established professional credentialing programs to enable individuals with the necessary level of expertise to provide effective oversight of work with all biohazardous materials, including BSAT. Additionally, the NIH has established the National Biosafety and Biocontainment Training Program (NBBTP) to formally train fellows in safe work practices required for research involving high consequence pathogens, and and/or high and maximum containment. The program provides the knowledge and experience required of biosafety professionals who manage or oversee work in these environments.[17]

Elevation of the biosafety program within an institutional governance structure helps to reinforce biorisk management principles by providing a mechanism for key program representatives to maintain direct communication with the institutional leadership (e.g., the Office of the Vice President for Sponsored Research in academia). Strategic assignment of positions within the organizational structure, which ensures an appropriate level of authority and autonomy to individuals responsible for biosafety and/or biosecurity oversight, demonstrates the institution's commitment to safe and responsible conduct of research, and to furthering improvements in the biorisk management program.

Modeling requirements articulated in the *NIH Guidelines*, the composition of the biosafety committee(s) should represent the breadth of research activities performed at the institution, in addition to other relevant stakeholders responsible for or involved in developing and implementing institutional biosafety and biocontainment programs. These include BSOs, SMEs in animal containment, physical containment, and laboratory technical staff involved in biological research at that institution.

APPROPRIATELY CONSTITUTED REVIEW ENTITY

In 2014, CDC's public report on the potential *Bacillus anthracis* exposures identified a number of confounding issues that led to the incident, and indicated that the "overriding factor contributing to this incident was the lack of an approved, written study plan reviewed by senior staff or scientific leadership to ensure that the research design was appropriate and met all laboratory safety requirements." CDC also noted other

[15] ABSA has two certification programs, the Certified Biological Safety Professional and Registered Biosafety Professional. Information is available at: http://www.absa.org/biocert.html.
[16] Information of the ASM NRCM program is available at: http://www.asm.org/index.php/certification/nrcm.
[17] Information on the NBBTP program is available at: http://www.nbbtp.org.

contributing factors including: "use of unapproved sterilization techniques, transfer of material not confirmed to be inactive, use of pathogenic *B. anthracis* when non-pathogenic strains would have been appropriate for this experiment, inadequate knowledge of the peer-reviewed literature" and the "lack of a standard operating procedure or process on inactivation and transfer to cover all procedures done with select agents in the Bioterrorism Rapid Response and Advanced Technology laboratory."[18]

Recommendation 1.3

- **Require that an appropriately constituted and qualified review entity[19] validate local policies, laboratory protocols, and mitigation plans involving the inactivation, sterilization, or decontamination of biohazardous materials at research institutions.**

CDC identified the use of a new and unvalidated protocol to inactivate *B. anthracis* as a primary cause for the accidental transfer and release of the live agent. This incident demonstrated that validation of SOPs for inactivation, sterilization, and decontamination of biohazardous materials is a critical component of a comprehensive biological risk assessment and mitigation plan. The FSAP developed guidance, *Non-viable Select Agents and Nonfunctional Select Toxins and Rendering Samples Free of Select Agents and Toxins*, which indicates that "A select agent or toxin must not be treated as non-viable or nonfunctional until it has been subjected to a method that has been validated to be effective on a specific agent or toxin. The burden of validating non-viability and non-functionality remains on the individual or entity possessing the select agent, toxin, or regulated nucleic acid."[20]

While BSAT biosafety plans include information for the safe and effective management of infectious waste, there are no similar provisions for non-BSAT programs. As a result, policies governing the management of infectious laboratory waste in these institutions vary significantly, which emphasizes the need to validate protocols associated with specific procedures and agents to ensure the safety of laboratory workers and the protection of public health. To address this issue, the FESAP recommends that an

[18] *Report on the Potential Exposure to Anthrax*, Centers for Disease Control and Prevention, July 11, 2014 is available at http://www.cdc.gov/about/pdf/lab-safety/Final_Anthrax_Report.pdf.

[19] An example of an appropriately constituted review entity is the Institutional Biosafety Committee (IBC, as described in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* [*NIH Guidelines*]) or its equivalent. The role of the IBC has expanded at many institutions. *The NIH Guidelines* is available at: http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.

[20] The FSAP guidance, *Non-viable Select Agents and Nonfunctional Select Toxins and Rendering Samples Free of Select Agents and Toxins,* is available at: http://www.selectagents.gov/guidance-nonviable.html

institutional biosafety program require validation of all SOPs for the inactivation, sterilization, and decontamination of infectious agents and toxins that includes a risk assessment and critical expert reviews of the data generated as part of the validation process.

The risk assessment process is intended to be a collaborative effort involving research personnel and institutional biosafety program staff that includes a comprehensive review of various processes involving agent manipulation, inactivation, sterilization, and/or associated decontamination procedures. Further, changes to the experimental design should require an additional review of inactivation, sterilization, and decontamination procedures when the design change may impact the handling of the agent or the necessary protocols.

Although additional review ensures expertise specific to both the protocol and the safe handling of the agent is brought to bear, it remains the responsibility of the PI to carefully examine the possible ramifications of any changes to experimental design. Collaboration between the PI and biosafety program personnel is important whenever the experimental design is altered in order to update the risk assessment and to identify any potential necessary changes in protocols resulting from that review.

Biosecurity and Security Awareness

Laboratory biosecurity refers to the protection of hazardous biological agents, including toxins, from loss, theft, diversion, or intentional misuse. Biosecurity is achieved through a combination of practices including the education and training of laboratory personnel, security risk assessments, personnel reliability measures, physical security (facility) safeguards, and the regulated transport of BSAT. Achieving effective, comprehensive biosecurity for BSAT is a shared responsibility throughout all levels of the research enterprise and oversight systems. Although the biosecurity measures and oversight responsibilities of the Federal Government are essential, facilities and individuals that possess, use, or transfer BSAT also play significant roles.

Biosecurity awareness and outreach are important for the safe and responsible conduct of high and maximum containment research. Meeting this objective will require the development and enhancement of existing biosecurity threat awareness programs beyond that offered in current biosafety training programs. Biosecurity awareness training is currently a required component of select agent training. The FESAP notes that it is possible to encourage the inclusion of security awareness training into the curricula of workers and scientists, as well as to incorporate biosecurity awareness into scientific ethics training in general and/or general biosafety training. It is important to note that

biosecurity awareness programs have the added benefit of reinforcing compliance and adherence to existing biosafety protocols and procedures.

SECURITY AWARENESS EDUCATION PROGRAMS/CURRICULUM DEVELOPMENT

Support for laboratory security awareness programs would foster a deeper understanding of the potential threats and promote basic security awareness in the life sciences community.

Recommendation 1.4

- **Support the development and implementation of security awareness education programs/curriculum that:**
    - **Underscore personal responsibility for safeguarding potentially hazardous biological agents;**
    - **Share information about security breaches that have occurred involving infectious or toxic materials;**
    - **Emphasize the need for self and peer reporting;**
    - **Discuss material protection strategies; and**
    - **Explain exploitation of life sciences research.**

The Federal Bureau of Investigation (FBI) Weapons of Mass Destruction Directorate currently conducts outreach to the life sciences community, including regulated entities registered with the FSAP, to provide training and education on security and threat awareness. The goal of these outreach programs is to effectively identify, prevent, and mitigate potential threats to personnel, research, materials, and facilities. These efforts have established strong, sustainable relationships throughout all levels of the research community (e.g., administration officials, compliance officers, staff, faculty, students), as well as with security and law enforcement stakeholders. The FBI brings a unique law enforcement perspective to its outreach program that focuses on threats posed by persons and organizations with the capabilities to damage or exploit the life science and public health communities or their infrastructures. The FBI approach to outreach is also unique in that it incorporates security and law enforcement equities, recognizing that they play a key role in preventing, detecting and responding to threats in the life sciences.

Key topics covered in the FBI's biosecurity outreach efforts include:

- Historical and security rationales for the implementation of the SAR, Biological Weapons Anti-Terrorism Criminal statutes, Biological Weapons and Toxins Convention, and U.N. Security Council Resolution 1540;

- Description of the threat and risk spectrum with case studies covering dual use/criminal misuse, domestic/international terrorism, espionage, intellectual property theft, cyber threats, insider threat/workplace violence and sabotage of critical research and public health efforts;
- Shared roles and responsibilities of the science and security/law enforcement communities in safeguarding the life sciences to include establishing effective lines of communication and notification protocols, sharing information to identify threat mitigation opportunities, and assisting with threat assessments;
- Role of the FBI in engaging the life sciences community to support preventive activities and assess/respond to reported suspicious and/or criminal activity.

The FBI Biosecurity Outreach Program has succeeded in fostering a much deeper understanding of potential threats and promoting basic security awareness in the life sciences community. Through greater awareness of the types of threats that may be present in the biomedical sector and key indicators that can be used to identify and assess those threats, institutions are implementing robust threat mitigation measures. Enhanced security awareness has also served to reinforce adherence to existing compliance measures directly addressing the "familiarity breeds contempt" vulnerability.[21]

The expansion of the FBI's and other outreach and education programs and the creation of similar programs at individual institutions would broaden the culture of security awareness and amplify existing efforts. Institutionally driven efforts can leverage aspects of relevant institution-specific research, culture, and structure to enhance understanding of biosecurity issues with methods tailored to the institutional audience. The combination of national and local programs to enhance biosecurity awareness would create a comprehensive framework of education in laboratories.

Biosafety

Biosafety refers to the application of a combination of laboratory practices and procedures, laboratory facilities, laboratory equipment, and appropriate occupational safety and health programs when working with potentially infectious agents and toxins. Current biosafety and biocontainment practices and procedures are designed to reduce the exposure of laboratory personnel, the public, animals, agriculture, and the environment to potentially infectious agents and other biological hazards. The key principles of biosafety

[21] See http://www.aaas.org/cstsp/programs/bridging-science.

include risk assessment and containment. The principles of biosafety and biocontainment have been articulated in two key reference documents, the *NIH Guidelines* (first published in 1976) and the *BMBL* (initially issued in 1984). In addition, engineering controls, facility design, use of safety equipment including primary barriers, administrative and work practice controls, and personal protective equipment (PPE) contribute to biosafety program effectiveness. None of these biosafety program elements can be effective, however, without thorough and frequent training.

BIOSAFETY AWARENESS

CDC released the findings of its internal investigation regarding the Spring 2014 incident of inadvertent cross-contamination of LPAI A (H9N2) virus sample with HPAI A (H5N1) virus and the subsequent shipment of the contaminated culture to an external high-containment laboratory. CDC found that there was a lack of awareness and understanding regarding reporting requirements for select agents, such as HPAI H5N1, that contributed to the delay in reporting this incident, as well as the failure to follow prescribed SOPs. This incident highlights the importance of biosafety awareness.

Recommendation 1.5

- **Develop and implement strategies to ensure effective communication and awareness of biosafety and biocontainment**

Biosafety awareness and training are essential to the safe and responsible conduct of life sciences research. Federal departments and agencies with responsibility for biosafety oversight have taken steps to ensure that constituency groups and collaborators in the academic and private sectors are aware of biosafety regulations and guidelines, informed about changes to regulations and guidelines, and understand the importance of compliance with established regulations and guidelines. These efforts to promote biosafety awareness vary among federal entities, but can include posting relevant biosafety information online, encouraging participation at conferences and meetings, and conducting outreach and distributing educational materials to program stakeholders. The FESAP recommends that the Federal Government continue to support and enhance awareness of the importance of laboratory biosafety. The effort should promote awareness among all individuals who work in, oversee, or manage research and provide training to address the importance of compliance with safety practices to minimize the risk of laboratory acquired infections and to protect the laboratory worker, the public, and agriculture.

APPLIED BIOSAFETY RESEARCH

As demonstrated in the 2014 CDC incident involving the use of an unsubstantiated inactivation protocol for *B. anthracis*, a clear need exists for increased applied biosafety research to validate laboratory protocols involving infectious agents and toxins, to create additional evidence-based practices and technologies, and to augment existing practices in order to reduce biohazard risks. These are ongoing processes, since laboratory biosafety protocols need to evolve in conjunction with technological advances.

Sustained support is needed for an applied biosafety research program that can address gaps in knowledge (engineering, PPE, sustainability of high containment facilities, and molecular mechanisms to enhance safety). For example, the development and validation of attenuated virus models to supplant intact pathogenic viruses would reduce risks and enable the use of lower biosafety level[22] conditions (e.g., Biosafety Level-2 [BSL-2] instead of BSL-3 or BSL-4) without compromising important research directed towards understanding how these infectious agents cause disease. The wider application of molecular safety controls in laboratory viruses may also provide an enhanced safety profile for research studies on microorganisms in high and maximum containment laboratories.

Practices and procedures, engineering controls, and PPE used in high and maximum containment research laboratories are based primarily on the results of studies performed decades ago, such as those involving equipment performance testing, disinfection, decontamination, and sterilization. Today, there are extremely limited resources directed towards developing new, evidence-based information regarding biosafety and biocontainment practices and procedures, engineering controls, and risk-assessment methodology. Support for this much-needed area of research will yield evidence-based improvements in biosafety practices, procedures, engineering controls, protective equipment, and facility design that will enhance the safety of biological laboratories.

Recommendation 1.6

- **Develop and maintain a robust federally-supported program of applied biosafety research to create additional evidence-based practices and technologies, and to update existing practices and operations.**

Currently, there are examples of small-scale applied biosafety research efforts, including research supported by the NBBTP. The NBBTP program offers two-year post baccalaureate and post-doctoral fellowships at the NIH campus that provide the opportunity to receive professional training in biosafety and biocontainment, and for the

[22] A biosafety level is a designation of a laboratory in ascending order based on the risk associated with the work being conducted.

conduct of applied biosafety research. The program fellows conduct applied biosafety research as part of training, but research is not the sole focus of the fellowship. In 2013, the Southeast Poultry Research Laboratory received funding for a Postdoctoral Research Associate to focus on applied biosafety research related to developing or validating processes to decontaminate equipment, rooms, and materials from avian viruses including HPAI viruses and Newcastle disease virus.

Despite the existence of a limited number of programs, there is no coordinated and comprehensive applied biosafety research effort. Therefore, the FESAP recommends the expansion of applied biosafety research efforts. With such an approach, applied biosafety research results have the potential to be shared widely through professional meetings, manuals, SOPs, and publications[23] in a timely manner that would improve the safe conduct of ongoing research efforts. Consideration should be given to the consolidation of information gained from these studies, and expansion of efforts to ensure the effective communication of such applied biosafety research results. This may include the need for an USG entity to develop an information resource (e.g., a clearinghouse for the collection and dissemination of biosafety and biocontainment applied research results).

INCIDENT REPORTING SYSTEM

Recent incidents involving BSAT have raised serious concerns:

- In Spring 2014, a LPAI A (H9N2) virus sample from a CDC influenza laboratory was inadvertently cross contaminated with the HPAI A (H5N1) virus, followed by the subsequent shipment of the contaminated culture to an external high-containment laboratory.
- In June 2014, an incident involving the potential exposure of staff to a pathogenic strain of *B. anthracis* at CDC laboratories occurred.
- On July 1, 2014, vials labeled ”variola,” the virus responsible for smallpox disease, were found in a cold storage room in an FDA laboratory located on the Bethesda campus of the NIH.

These recent incidents highlight the importance of minimizing the potential for future events. The development of a voluntary, non-punitive incident reporting system could enable trend analysis, sharing of lessons learned, and ultimately contribute to the minimization of future incidents.

Recommendation 1.7

[23] *Applied Biosafety: Journal of the American Biological Safety Association* (ISSN 1535-6760) is a “peer-review scientific journal committed to promoting global biosafety awareness and best practices to prevent occupational exposures and adverse environmental impacts related to biohazardous releases.” See http://www.absa.org/pubabj.html.

- **Establish a new voluntary, anonymous, non-punitive incident-reporting system for research laboratories that would ensure the protection of sensitive and private information, as necessary.**

Prompt and detailed reporting of laboratory incidents and exposures and potential breaches of biosafety involving research with potentially hazardous microorganisms and biological toxins is essential to optimizing laboratory safety and oversight. While OSHA, FSAP, and the NIH Office of Biotechnology (OBA) activities outline requirements for laboratory incident reporting for relevant entities, there is no centralized, integrated incident reporting and analysis system for incidents occurring in all U.S. biological research facilities in all sectors. The importance of incident reporting is emphasized in the testimony of Dr. Thomas Frieden, CDC Director, before the House Energy and Commerce Subcommittee on Oversight and Investigations on July 16, 2014, in which he indicated that "We also need to encourage a culture of openness and effective reporting of past or future incidents – since a key aspect of effective response is to support rapid reporting of problems."[24]

Therefore, the FESAP supports the establishment of a voluntary, anonymous, non-punitive, incident-reporting system for laboratory acquired infections, near misses or other incidents that enables analyses, lessons learned from all research laboratories in all sectors, and information-sharing regarding incidents.

It is important to note that an anonymous, non-punitive incident reporting system would not supplant existing mandatory reporting requirements. While there may be debates over the definition of an incident, a working definition of "incident" as it relates to laboratories working with infectious agents should include both laboratory-acquired infections (LAIs) as well as potential exposures and near misses, and take into consideration incidents in the agriculture and public health sectors (i.e., a one health approach). At present, better medical surveillance and reporting of LAIs and other incidents and response is needed. Analyses of reports of biosafety and biocontainment incidents, or lack of adherence to recommended safety practices could also point to the need for areas of enhanced training, new or revised guidelines or practices, and site visits or inspections. In addition, when compiled, appropriately analyzed, and communicated, these data would provide essential information for public education and outreach.

Currently, several small scale agency-specific pilot projects are addressing the need for incident reporting. For example, the FSAP has implemented a hotline to report incidents,

[24]See: http://energycommerce.house.gov/hearing/review-cdc-anthrax-lab-incident.

with whistleblower protections. Similarly, OSHA has a Whistleblower Protection Program that protects employees (http://www.whistleblowers.gov/index.html), and the USDA has a Whistleblower Protection Ombudsman in the OIG at Ombudsman@usda.oig.gov for both employees and the public. FSAP submits information on select agent theft, loss and release to Congress. CDC also publishes the results of national select agent theft, loss, and release.[25] However, a pilot incident reporting system could be developed to encompass the spectrum of these incidents with the goal of minimizing future incidents.

A potential model for an incident-reporting system is the voluntary, non-punitive, centralized system used by the aviation industry. It promises anonymity and guarantees the Federal Aviation Administration (FAA) "... will not use reports submitted to the National Aeronautics and Space Administration (NASA) under the Aviation Safety Reporting Program (or information derived therefrom) in any enforcement action, except information concerning accidents or criminal offenses which are wholly excluded from the program."[26] A second incident-reporting system that could be used as a model is the U.S. HHS Agency for Healthcare Research and Quality (AHRQ) Patient Safety Organization-Network of Patient Safety Databases.[27]

Inventory Management and Control

The *BMBL*, produced jointly by CDC and NIH, has been the most widely used technical reference in the United States for laboratory biosafety and biocontainment principles for decades. The *BMBL* is the standard for best practices. Section 6 the BMBL provides guidance and expectations on proper material accountability procedures:

> Material accountability procedures should be established to track the inventory, storage, use, transfer and destruction of dangerous biological materials and assets when no longer needed. The objective is to know what agents exist at a facility, where they are located, and who is responsible for them. To achieve this, management should define: 1) the

[25] Richard D. Henkel, Thomas Miller, and Robbin S. Weyant. Monitoring Select Agent Theft, Loss and Release Reports in the United States—2004-2010. *Applied Biosafety* Vol. 17, No. 4, 2012, www.absa.org

[26] This centralized, incident-reporting system is used by the National Transportation Safety Board, and was first developed by the FAA in 1975. FAA then transferred authority for its Aviation Safety Reporting Program to NASA (see http://asrs.arc.nasa.gov/). For more information about immunity provisions in the FAA/NASA incident-reporting system, see: http://asrs.arc.nasa.gov/overview/immunity.html.

[27] This program has a legislative framework under the Patient Safety and Quality Improvement Act of 2005(Public Law 109-41). For additional information about HHS AHRQ Patient Safety Organization-Network of Patient Safety Databases, see: http://www.pso.ahrq.gov/.

materials (or forms of materials) subject to accountability measures; 2) records to be maintained, update intervals and timelines for record maintenance; 3) operating procedures associated with inventory maintenance (e.g., how material is identified, where it can be used and stored); and 4) documentation and reporting requirements.[28]

The efficient and effective management of BSAT inventories ensures that all BSAT are properly controlled, registered, and accounted for with the FSAP. Inventory of BSAT is currently regulated by the FSAP as outlined in SAR (7 CFR Part 331, 9 CFR Part 121 and 42 CFR Part 73) which outlines specific information to be captured.

Sections 11 (Security) and 17 (Records) of the SAR outlines requirements for select agents in long term storage and toxins that deter and detect a variety of insider threats, including provisions on inventory audits and records management. The requirements include:

- Current accounting of any animals or plants intentionally or accidentally exposed to, or infected with, a select agent;
- An accurate and current inventory of each select agent or toxin;
- Labeling and identifying select agents and toxins in the entity inventory in a way that leaves no question that the entity's inventory is accurately reflected in the inventory records;
- Accounting for select agents and toxins from acquisition to destruction; and
- Accounting for select agents and toxins as they are withdrawn from storage and returned to storage.

The FSAP has provided guidance related to inventory management and control as part of its Security Guidance document,[29] and "Guidance on the Inventory of Select Agents and Toxins" document.[30]

Section 11 (Security) of the SAR, specifies that entities must conduct complete inventory audits of Tier 1 select agents and toxins in long-term storage when any of the following occur:

---

[28] BMBL, 5th edition, "Elements of a Biosecurity Program", page 109. The online fifth edition of the *BMBL*, developed by NIH and CDC is available at: http://www.cdc.gov/biosafety/publications/bmbl5/index.htm.

[29] The FSAP has guidance as part of its overall Security Guidance document. The Guidance is available at: http://www.selectagents.gov/resources/Security_Guidance_v3-English.pdf)

[30] The FSAP's guidance document specifically addressing the long-term storage of select agents and toxins is available at http://www.selectagents.gov/resources/Long_Term_Storage_version_5.pdf.

- "Upon the physical relocation of a collection or inventory containing select agents and toxins. This includes moving a collection or inventory into a new facility or into a new storage location within the same facility;
- Upon the departure or arrival of a PI for select agents or toxins under the control of that PI; or
- In the event of a theft or loss of a select agent or toxin, all select agents and toxins under the control of the PI that suffered the theft or loss."

As inventory management and control is addressed in federal regulations and guidance, it is also addressed in USG departments' and agencies' policies and directives.

The USDA sets forth policies for inventory management and control in its Security Policies and Procedures for Biosafety, as defined in DM9610.001 for BSL-3, and in DM9610.002 for non-containment laboratories. The Inventory Control section describes policy on the handling, storage, shipping, disposal, record keeping, and monitoring of all biological agents. The intent of this section is also to ensure proper chain-of-custody procedures are utilized. There are three types of accountability records that are required for USDA facilities, including the National Pathogen Inventory (NPI) system, a detailed inventory of repository materials to be kept at the research or diagnostic facility, and materials accountability for experimental or working samples:

- NPI. Agencies will maintain a summary inventory database to provide management with the capability to rapidly determine pathogens in use at each facility. NPI is maintained by the Agricultural Research Service (ARS) at each ARS location and at Headquarters. ARS also maintains this information for other USDA agencies and each USDA agency validates this information annually.

- Facility Inventory of Repository Materials. Each USDA facility that stores or uses any pathogen must maintain a current detailed inventory. Each facility will maintain a current master database reflecting the cumulative pathogens of all management units at the facility. The database serves as a record of current inventory but will also serve as a historical record of pathogens used at the facility.

- Material Accountability of Experimental or Working Samples. Experimental samples and repository stock aliquots used for working stocks or experimental purposes are tracked by laboratory records (laboratory notebooks, electronic systems, etc.). The location of material use must be included. At the conclusion of each experiment, the disposition of the infectious material, including the

means of disposal, must be verified by the signature of the researcher or diagnostician, or a designee.

Physical Review of Accountability Records. Within USDA, scientists working with pathogens are responsible for the accuracy of electronic databases and laboratory notebook records, which are subject to review by a supervisor, the laboratory director, and authorized agency personnel. A physical review is required at least annually. Methods used during physical review or reconciliation may include counts of the entire inventory or statistical sampling of records and repository materials. The center director, laboratory director, or equivalent is responsible for ensuring the physical reviews are accomplished. Random reviews shall be conducted on an annual basis by the agency BSO to ensure compliance at the locations.

DHS, in Management Directive (MD) 026-03 'Select Agent and Toxin Security,' issued general guidance pertaining to inventory requirements. In Section VI Policy and Procedures: "Proper storage, management, and safeguards which may be issued by the Department, will be used to prevent loss, theft, diversion, damage, and unauthorized use of all select agents and toxins."[31] Additionally, security controls, as required by Authorities D-F at Part III of this MD, shall be provided against unauthorized access; "Select agents and toxins shall be actively monitored and accounted for from identification through transfer and final disposition, to include destruction, via the employment of stringent property control processes including the execution of chain-of-control documentation and destruction logs."

Recently, all USG departments and agencies were tasked by the White House (August 18, 2014, memo on enhancing biosafety and biosecurity) to "kick-off" an immediate sweep of facilities that possess, use, or transfer infectious human, animal, or plant agents or toxin holdings to identify BSAT that may be inappropriately stored.[32] This also provided an opportunity to assess current compliance levels and lessons learned. Departments and agencies recommended many best practices that should be encouraged. Best practices included: 1) the development of a quality assurance mechanism to ensure proper possession, use, tracking, monitoring and transfer of BSAT; and 2) the development of and adherence to a mechanism to ensure biological material ownership and responsibility is transferred when an individual leaves the organization.

[31] DHS Management Directive 026-03 'Select Agent and Toxin Security' is available at: http://www.dhs.gov/publication/management-directives-volume-0000-general-management-and-administration.

[32] The August 18, 2014 White House memo on enhancing biosafety and biosecurity is available at: http://www.whitehouse.gov/sites/default/files/microsites/ostp/enhancing_biosafety_and_biosecurity_19aug2014_final.pdf.

In addition, various groups including ASM provided guidance to members on the importance of documenting and maintaining proper inventory practices. In the guidance document "What is in your Laboratory Freezer?" ASM sent a statement to ASM members reminding them to practice safe "laboratory housekeeping."[33]

MATERIAL ACCOUNTABILITY

The goal of efficient and effective management of BSAT inventory is to ensure that all BSAT are controlled properly, registered, and accounted for with the FSAP. At present, there are 317 entities registered to work with BSAT, but inventory management and control mechanisms vary among the entities, often for infectious agents/toxins- or research-specific reasons. While the BSAT regulations provide specific guidance on inventory management, there is the possibility that aged, historical samples or collections have been "orphaned" and therefore not properly identified and registered with the FSAP. For example, on July 1, 2014, vials labeled "variola," the causative agent of smallpox, were discovered in a storage room in a FDA laboratory located on the NIH Bethesda campus. Consequently, increased awareness of existing guidance and regulations is needed to prevent similar occurrences in the future is required.

Recommendation 1.8

- **Increase awareness about existing material accountability best practices, and support the establishment of material accountability procedures where none currently exist.**

The FESAP noted that adherence to SAR and other guidance documents are important for good laboratory practices and for reinforcing a culture of responsibility. Adherence to these guidelines ensures that institutions know what agents exist at a facility, where they are located, and who is responsible for them. Accountability, including development and implementation of mechanisms to ensure continued management and control of inventory when an investigator leaves an institution, is essential to safe and effective management of all research involving potentially hazardous biological materials.

In the event that additional biological agents are added to the select agent list, a strong system for ensuring compliance would include an efficient mechanism to rapidly incorporate newly regulated biological agents and toxins into the existing system.

[33] See http://www.asm.org/index.php/whatsnew-policy/99-policy/policy/93059-freezer-8-14.

III. IDENTIFICATION OF ACTIONS AND ANY REGULATORY CHANGES TO IMPROVE BIOSAFETY AND BIOSECURITY

The FESAP was charged to identify actions and regulatory changes to improve biosafety and biosecurity. The FESAP considered the SAR, which implement Title II, Subtitle A and Subtitle B (also known as the Agricultural Bioterrorism Protection Act of 2002) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and set forth the requirements for the possession, use, and transfer of select agents and toxins.[34] The SAR can be found at 42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331. The FESAP proposed changes to the SAR, enhancements to the select agent regulatory guidance, and supported another proposed regulatory tool for expanded federal oversight beyond BSAT.

BACKGROUND

Charge

To strengthen USG oversight of work with infectious agents, including (but not limited to) BSAT, the White House NSC requested that the FESAP undertake a comprehensive federal review that would result in specific recommendations to strengthen the Government's biosafety and biosecurity practices and oversight system for federally-funded activities, consistent with the need to realize the public health and security benefits of such work. More specifically, with respect to federally-funded activities, the FESAP was asked to identify actions and any regulatory changes to improve biosafety and biosecurity.

Scope

The scope of activities considered by the FESAP for this section of the report includes those laboratory research activities in all sectors utilizing BSAT but also addresses non-BSAT. Activities that take place in diagnostic and treatment (non-research) facilities such as hospitals, clinics, veterinary, and food diagnostic laboratories are beyond the scope of the FESAP. The recommendations in this section of the report specifically focus on recommended changes to improve biosafety and biosecurity and address the SAR and associated guidance documents, as well as federal oversight beyond BSAT.

[34] Information about the SAR is available at: http://www.selectagents.gov.

Approach

To address the need for potential regulatory changes necessary to improve biosafety and biosecurity, the FESAP considered the following questions:

- Should the SAR be modified to improve biosafety and biosecurity management and control? If so, what modifications should be proposed?
- Should regulatory oversight be applied to improve biosafety and biosecurity management and control of biological pathogens and toxins that are not considered to be BSAT?
- Are there other regulations or guidelines that can be modified to improve biosafety and biosecurity management and control of biological pathogens and toxins (BSAT and non-BSAT)?

In addressing these questions, FESAP received briefings on the following topics:

- The 2012 amendments to the SAR
- The *BMBL* and its relationship to the SAR
- The Canadian Human Pathogens and Toxins Act
- The Maryland state regulations governing select agent possessors
- The OSHA standards and regulations most applicable to work with BSAT, other biological pathogens and additional laboratory hazards:
    - The Bloodborne Pathogens standard (29 C.F.R. § 1910.1030)
    - The Personal Protective Equipment standard (29 C.F.R. § 1910.132)
    - The Respiratory Protection standard (29 C.F.R. § 1910.134)
    - The Accident Prevention Signs & Tags standard (29 C.F.R. § 1910.145)
    - The General Duty Clause (29 U.S.C. § 654)
    - The Hazard Communication standard (29 C.F.R. § 1910.1200)
    - The Occupational Exposure to Hazardous Chemicals in Laboratories standard (Laboratory standard)(29 C.F.R. § 1910.1450)
- A regulatory framework for an OSHA Infectious Diseases (ID) standard to protect workers from exposure to infectious agents transmitted by the contact, droplet and airborne routes.

Department and agency representatives submitted suggestions for proposed amendments to current regulations, primarily the SAR, to the working group co-chairs. These suggestions were collated into three matrices and discussed by the working group. Those

suggestions that obtained support were incorporated into recommendations of the FESAP.

IDENTIFICATION OF ACTIONS AND ANY REGULATORY CHANGES TO IMPROVE BIOSAFETY AND BIOSECURITY OVERSIGHT

Proposed Changes to the SAR

A number of suggested amendments were considered in the process of arriving at proposed changes to the SAR. There was a general feeling within the FESAP working group that there already exists a very thorough framework to regulate the safe and secure handling of pathogens and toxins of concern. Furthermore, the events precipitating this review of our regulatory landscape are believed to have resulted from non-compliance with existing regulations, rather than a lack of existing regulations. The FESAP thus does not see the need for sweeping changes to the current SAR and other guidance documents, but does recognize that this request for review provides an opportunity to suggest enhancements to the current regulatory landscape. Specific changes to the SAR recommended by FESAP follow.

Recommendation 2.1

- **Add a specific requirement for the documentation of the drills and exercises required in sections 11 (Security), 12 (Biosafety), and 14 (Incident Response) of the current SAR.**

A change recommended by the FESAP for the SAR includes adding a specific requirement for the documentation of the drills and exercises required in sections 11 (Security), 12 (Biosafety), and 14 (Incident Response) of the current SAR. Although the current regulations require that these drills and exercises be performed on an annual basis, there is no specific requirement for the documentation of these events. Adding a documentation requirement would improve the ability of the regulatory programs to assess the quality and comprehensiveness of these programs.

Recommendation 2.2

- **Add a specific requirement to section 15 (Training) to include how a trainee can access the HHS OIG Hotline to anonymously report a safety or security concern.**

A change recommended by the FESAP for the SAR includes adding a specific requirement to section 15 (Training) to include how a trainee can access the HHS OIG Hotline to anonymously report a safety or security concern. Under the current oversight mechanism, the primary communication link between a regulated entity and the FSAP is through the entity's RO. Although the FSAP has established a whistleblower portal on the FSAP website, there is currently no requirement for employees in BSAT programs to be made aware of this mechanism or how to use it. Adding this requirement could allow increased worker involvement in biosafety and biosecurity programs at BSAT facilities and could also enhance the quality of federal oversight in this area.

Proposed Enhancements to the Select Agent Regulatory Guidance

FESAP participants presented many suggestions for program improvement. For the most part, the group concluded that these would be best implemented through improvements to the current guidance documents provided by the FSAP.

Recommendation 2.3

- **Optimize guidance to address integration of the RO with the entity's biosafety and biosecurity oversight committee(s).**

A change recommended by the FESAP includes developing optimized guidance to address integration of the RO with an entity's biosafety and biosecurity oversight committees. Given the scope of the responsibilities of the RO in the SAR, it is important that this person has access to, and interacts with, all applicable entity safety and security oversight bodies. Multiple sections of the SAR require that security and incident response activities be well coordinated, both within the institution and with local law enforcement and/or first responders. In many regulated entities, this would include the local IBC. In recommending optimization of guidance rather than regulatory enhancement, the diversity in size and scope of regulated entities and the corresponding diversity in local oversight committees were considered.

Recommendation 2.4

- **Modify guidance documents to recommend that the composition of the local oversight committee(s) represent the breadth of stakeholders involved in developing and implementing institutional biosafety and biocontainment programs.**

A specific change recommended by the FESAP includes the modification of guidance documents to recommend that the composition of the local oversight committee(s) represent the breadth of stakeholders involved in developing and implementing institutional biosafety and biocontainment programs. A model for this type of best practice is provided by the *NIH Guidelines*, which mandates (or recommends in some cases) the composition of IBCs (e.g., BSO, members with expertise in research being performed such as animal containment, physical containment, and laboratory technical staff).

Guidance documentation should be amended to suggest overlapping representation on institutional oversight committees in order to enhance communication between committees at institutions that have multiple committees for oversight of different aspects of biosafety and biosecurity (e.g., BSAT, non-BSAT, recombinant and synthetic nucleic acid molecules, and non-recombinant molecules).

Recommendation 2.5

- **Improve guidance regarding working stocks and inventory control.**

A specific change recommended by the FESAP includes the development of improved guidance regarding working stocks and inventory control. The current FSAP guidance library contains information on inventory control in multiple documents (i.e., the long term storage and security guidance documents). The FESAP believes this information should be combined into a comprehensive inventory compliance guidance document that addresses all regulatory requirements in this area. Chapter II, Inventory Management and Control section of this report, provides additional information about material accountability.

Recommendation 2.6

- **Improve guidance for biosafety plans.**

A specific change recommended by the FESAP includes the development of improved guidance for biosafety plans. The current SAR is not specific in what types of information should be included in a regulated entity's biosafety plan. The FESAP believes that a guidance document should be developed to include what specific areas should be addressed by an entity in its BSAT biosafety plan. These areas should include: risk assessment, use of safety equipment, PPE, containment devices, and occupational health considerations. This would provide regulated entities with a useful bridge between the SAR and the biosafety standards referenced in the SAR (e.g., *BMBL* and *NIH Guidelines*).

Recommendation 2.7

- **Amend guidance documents to suggest that entities consider establishing policies on maximum work hours for high containment workers.**

A specific change recommended by the FESAP includes the amendment of guidance documents to suggest that entities consider establishing policies on maximum work hours for high containment workers. While there will likely be times of crisis when lengthy work schedules may be required to respond to national needs, there should be consideration for the risk versus benefit of asking workers to engage in extended work periods in high containment laboratory settings. It would be beneficial to develop policy or guidance on this matter. These considerations might include requiring the management to be notified of work outside regular business hours, and/or work beyond limited number of hours. Such policies could be beneficial to the workers as well as for biosafety and biosecurity of the laboratory.

Other Proposed Regulatory Tools for Expanded Federal Oversight Beyond BSAT

Recommendation 2.8

- **Support U.S. OSHA Infectious Diseases Standard.**

OSHA is currently drafting an Infectious Diseases standard that would address the hazards unique to working with infectious materials in laboratory and healthcare settings (Appendix D). This standard would complement current OSHA standards and regulations (e.g., Bloodborne Pathogens Standard, Personal Protective Equipment Standard, Laboratory Standard) and would apply the biosafety concepts of guidance documents such as the *BMBL* and *NIH Guidelines* to the broader U.S. workforce that may have occupational exposure to infectious diseases transmitted through contact, droplet and airborne routes. This effort should be considered for support by NSC and OSTP, and its development and implementation should be a high priority.

IV. IDENTIFICATION OF AN APPROACH TO DETERMINE THE APPROPRIATE NUMBER OF HIGH-CONTAINMENT U.S. LABORATORIES REQUIRED TO POSSESS, USE, OR TRANSFER BSAT

The White House NSC requested that the FESAP identify an approach to determine the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT.

BACKGROUND

Plant, animal, and human pathogens, whether disseminated by natural, accidental, or deliberate means, cause disease outbreaks that can lead to death and illness, economic damage, social disruption, and environmental contamination. Countering these disease agents requires studying mechanisms of pathogenesis, developing physical and medical countermeasures, and conducting surveillance, diagnosis, and other operational activities – which in turn require laboratory facilities in which these activities can be done safely.

Increases in the number of federal high and maximum containment laboratories over the past two decades have been driven by increased requirements for basic and applied research involving infectious agents and toxins, in response to world events such as epidemics and pandemics, biological attacks, and emerging and re-emerging infectious disease. Ultimately, the approach to determine the appropriate number (or space) for biocontainment laboratories needed by the U.S. Government depends on the current and future mission analysis and projection of need by federal departments and agencies. Federal departments and agencies with the mission of responding, or developing the capacity to respond, to such biological events have sought to ensure sufficient containment laboratory capacity in which to undertake research and development for countermeasures, development of diagnostic capabilities, and fundamental research on infectious agents and toxins. The questions that are being asked now, after these past investments have come to fruition, is whether the United States has too much, too little or just the right amount of space to address needs of the future. The basis for these types of questions is not restricted to the issues of the resource commitments during a time of fiscal austerity, but also from the presumption that expansion of biocontainment space increases the likelihood of an accident that could have broader agricultural or public health consequences.

Although protections are in place in laboratories, work with infectious agents and biological toxins inevitably involves some risk to the laboratory worker, public health, and agriculture. These risks are minimized by appropriate design, construction, and operation of the laboratories where this work is performed. However, the only way to completely eliminate these risks would be not to do the work at all, which presents a different set of risks – that diseases will not be detected or diagnosed, that treatments or mitigation measures will not be developed, or that disease outbreaks will not be controlled. The appropriate number of high containment U.S. laboratories necessary to possess, use, or transfer BSAT is the number of laboratories that departments and agencies have determined are required to safely and securely conduct the research, development, and operational activities to counter these disease agents, recognizing the risks that these facilities themselves may pose, together with consideration of any other factors that may be identified that pertain to the aggregate amount of containment laboratory space. This section of the report outlines an approach for determining the appropriate number of containment laboratories in the United States required to possess, use, or transfer BSAT.

Fundamental to this analysis is the recognition that the physical presence of high and maximum containment laboratories does not inherently either pose risk or confer benefit. The risks and benefits associated with these laboratories depend on the infectious agents and toxins studied within them; the nature of the activities being conducted (e.g., preparation and characterization of infectious agent and toxin materials, aerosol studies, animal and plant studies to evaluate pathogenicity, drug efficacy, etc.); the expertise and training of laboratory and related support staff; the human, animal and plant species being used; and the containment systems and strategies employed.

Scope

The FESAP identified the implied scope of the charge from the NSC to extend to research laboratories that are within the Federal Government's purview. Since the Federal Government has full internal control of and oversight responsibility for construction and operation of its own research laboratories, the scope of this analysis focuses on facilities that are built with federal funds, or that conduct federally-directed research activities. This report does not address commercial clinical laboratories and other non-research diagnostic and treatment facilities such as hospital, veterinary, plant and food diagnostic laboratories either because they support operational health or food safety missions that are largely under the responsibility of the private sector, or of state

and local Government, and are not amenable to direct federal control.[35] Non-research activities in most licensed biomedical production facilities and mobile field analytical laboratories also lie outside the scope of this report. Future FESAP reports may address those laboratories constructed and/or operated without federal funds.

The scope of containment facilities considered by FESAP cannot be defined simply as those that possess, use, or transfer BSAT, because non-BSAT containment space can potentially be modified to permit work with BSAT. A need exists to address all high containment facilities (government [federal, state, tribal, and municipal], academia, privately funded research institutions, private industry, and overseas facilities) potentially available for use for federally-funded activities that utilize potentially hazardous biological agents. The federal facilities covered include those conducting research with disease-causing agents (pathogens) that can infect humans, zoonotic agents that can infect both animals and humans, biologic toxins, and agricultural pathogens and pests.

Description of Biosafety Levels, Various Enhancements and Other Requirements to Meet Particular Research Needs

Biosafety levels (BSL) are designations of laboratories in ascending order based on the degree of risk associated with the work being conducted. The designations BSL-1, BSL-2, BSL-3, and BSL-4 are for work with human and zoonotic pathogens, and each represent certain combinations of engineering controls, facility design, safe work practices, and safety equipment. The "BSL" laboratory designation does not apply to plant pathogens. However, plant pathogens are typically contained in laboratories and greenhouse facilities with containment features that meet the requirements described for BSL-1, BSL-2 and BSL-3 laboratories. The plant biosafety (biocontainment) level designations are BL1-P, BL2-P, BL3-P, and BL4-P. Each combination is specifically appropriate for the operations performed, the documented or suspected routes of transmission of the infectious agents involved, and the laboratory function or activity. The assignment of a biosafety level to a particular work process or research protocol is made through protocol-driven risk assessment, so that potential hazards specific to the work can be identified and mitigated effectively.

"High and maximum containment" is the term used to describe BSL-3 and BSL-4 laboratories and equivalent animal or agricultural containment facilities (e.g., animal

[35] This report excludes clinical laboratories in federal health care facilities, even though they operate on federal funds, because any decision to increase or decrease such laboratory capacity would be incidental to broader health care policy decisions that are outside the scope of this analysis. However, it does include federal laboratories performing unique federal missions such as serving as reference diagnostic laboratories.

facility/vivarium Animal Biosafety Level (ABSL) -3 and ABSL-4, and biosafety level-3 agriculture (BSL-3Ag) facilities). More specifically, "high containment" refers to BSL-3 and equivalent containment facilities, whereas "maximum containment" refers to BSL-4 and equivalent containment facilities. The research activities that occur in high and maximum containment facilities include studies of hazardous pathogens that infect humans, zoonotic agents, toxins, and a range of agricultural pathogens, which include foreign and emerging agricultural agents that can infect livestock and crops.

Biosafety level 3 (BSL-3), or high-containment, laboratories are appropriate for work with human or animal pathogens with a known potential for aerosol transmission, those that can cause serious and potentially lethal infections, and for those that are not indigenous or are otherwise exotic in origin.[36] BSL-3 laboratories require specific laboratory practices, safety equipment, and facility safeguards. High containment is achieved by implementing various degrees of laboratory safety and security measures, through laboratory design and access restrictions (to the facilities, research materials and information), professional expertise and training, use of containment equipment, and application of safe methods of managing pathogenic materials in a laboratory setting.[37]

While biosafety level designations, as defined in the *BMBL*, refer to levels of containment rather than categories of facilities, for the purpose of this report, the facilities equipped with BSL-3 and BSL-4 containment measures are denoted as high-containment and maximum-containment laboratories, respectively.

The primary consideration in the design, construction, commissioning, validation, operation and maintenance of a BSL-3 laboratory is the assessment of risk involved in the proposed research, clinical, or manufacturing activity. While the simplest high-containment laboratory is a two-space facility with an entry door from an access corridor into an anteroom to the BSL-3 laboratory, multiple variants exist including as a stand-

[36] Laboratories involving research with biological materials are classified into four BSL categories (BSL1, BSL2, BSL3, and BSL4). These categories are outlined in detail in the Biosafety in Microbiological and Biomedical Laboratories (BMBL) issued by the CDC and NIH. The *NIH Guidelines* similarly describe four levels of biocontainment (BL1 to BL4), which closely parallel those described in the *BMBL*. Animal research facilities are classified into four animal biosafety level (ABSL) categories (ABSL1, ABSL2, ABSL3, and ABSL4).

[37] Both NIH and ARS issued standards for design of such facilities (including considerations for construction,, commissioning, operations, and decommissioning), available at: http://orf.od.nih.gov/PoliciesAndGuidelines/BiomedicalandAnimalResearchFacilitiesDesignPoliciesandGuidelines/Documents/Design%20Requirements%20Manual/NIH%20Design%20Requirements%20Manual%20ver%205-13.pdf and http://www.afm.ars.usda.gov/ppweb/PDF/242-01M.pdf, respectively. In addition, A new standard, **ANSI/ASSE Z9.14**, was recently released; it provides a voluntary but systematic approach to evaluate safety design features, as well as operations and engineering processes and controls in high-containment laboratories and animal facilities (see: http://www.alnmag.com/articles/2014/01/ansi-z914-ansi/asse-z914-implications-animal-facilities).

alone BSL-3 laboratory suite, multiple BSL-3 spaces served by one anteroom or with a BSL-2 laboratory as access area.[38] The diversity in the design of high containment laboratories enables research with a diversity of species (e.g., insects, plants, animals, etc.)

Table 1 summarizes the recommended biosafety levels, including biosafety practices, primary barriers and protective equipment, and facility safeguards associated with the various biosafety containment levels for working with pathogens that are infectious to humans.

TABLE I

SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR HUMAN INFECTIOUS AGENTS[39]

BSL	AGENTS	PRACTICES	PRIMARY BARRIERS AND SAFETY EQUIPMENT	FACILITIES (SECONDARY BARRIERS)
1	Not known to consistently cause diseases in healthy adults	Standard Microbiological Practices	None required	Laboratory bench and sink required
2	• Agents associated with human disease • Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: • Class I or II BSCs* or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPE§: • Laboratory coats; gloves; face protection	BSL-1 plus: • Autoclave available

[38] Crane, J. and Riley, JF. Design of BSL3 Laboratories (Chapter 7 of *Anthology of Biosafety I: Perspectives on Laboratory Design*). American Biological Safety Association.1999.
[39] Table 1 has been reprinted from the *BMBL*, fifth edition, Section IV.

			as needed	
3	• Indigenous or exotic agents with potential for aerosol transmission • Disease may have serious or lethal consequences	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of laboratory clothing before laundering • Baseline serum	Primary barriers: • Class I or II BSCs or other physical containment devices used for all open manipulation of agents PPE: • Protective laboratory clothing; gloves; respiratory protection as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhaust air not recirculated • Negative airflow into laboratory
4	• Dangerous/exotic agents which pose high risk of life-threatening disease • Aerosol-transmitted laboratory infections have occurred; or related agents with unknown risk of transmission	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	Primary barriers: • All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit	BSL-3 plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum, and decontamination systems • Other requirements as outlined in *BMBL* text

[*] BSC – Biosafety Cabinet

[§] PPE – Personal Protective Equipment

Table 2 summarizes the recommended biosafety levels (including biosafety practices, primary barriers and protective equipment, and facility safeguards associated with the various biosafety containment levels) for the containment of agents that can infect vertebrate animals other than humans.

TABLE 2

SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR ACTIVITIES IN WHICH EXPERIMENTALLY OR NATURALLY INFECTED VERTBRATE ANIMALS ARE USED[40]

ABSL	AGENTS	PRACTICES	PRIMARY BARRIERS AND SAFETY	FACILITIES (SECONDARY

[40] Table 2 has been reprinted from the *BMBL*, fifth edition, Section V.

			EQUIPMENT	BARRIERS)
1	Not known to consistently cause diseases in healthy adults	Standard animal care and management practices, including appropriate medical surveillance programs	As required for normal care of each species	Standard animal facility: • No recirculation of exhaust air • Directional air flow recommended • Hand washing sink is available
2	• Associated with human disease • Hazard: percutaneous exposure, ingestion, mucous membrane exposure.	ABSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual • Decontamination of all infectious wastes and of animal cages prior to washing	ABSL-1 equipment plus primary barriers: • Containment equipment appropriate for animal species PPE[§] : • Laboratory coats, gloves, face and respiratory protection as needed	ABSL-1 plus: • Autoclave available • Hand washing sink available • Mechanical cage washer recommended
3	• Indigenous or exotic agents with potential for aerosol transmission • Disease may have serious health effects	ABSL-2 practice plus: • Controlled access • Decontamination of clothing before laundering • Cages decontaminated before bedding removed • Disinfectant foot bath as needed	ABSL-2 equipment plus: • Containment equipment for housing animals and cage dumping activities • Class I, II or III BSCs available for manipulative procedures (inoculation, necropsy) that may create infectious aerosols. PPE: • Appropriate respiratory protection	ABSL-2 facility plus: • Physical separation from access corridors • Self-closing, double-door access • Sealed penetrations • Sealed windows • Autoclave available in facility
4	• Dangerous/exotic agents that pose high risk of life threatening disease • Aerosol transmission, or related agents with unknown risk of transmission	ABSL-3 practices plus: • Entrance through change room where personal clothing is removed and laboratory clothing is put on; shower on exiting • All wastes are decontaminated before removal from the	ABSL-3 equipment plus: • Maximum containment equipment (i.e., Class III BSC[*] or partial containment equipment in combination with full body, air-supplied positive-pressure personnel suit) used for all procedures and activities	ABSL-3 facility plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum and decontamination systems • Other requirements outlined in the text

		facility		

[*] BSC – Biosafety Cabinet

[§] PPE – Personal Protective Equipment

Characteristics of High/Maximum-Containment Laboratory Space

Decisions to build biocontainment space are not taken lightly because of the great time and expense that must be devoted to achieve a facility that complies with all regulatory requirements and that can be efficiently used and maintained. Because of the time lag inherent in constructing such facilities, departments and agencies cannot assume that space will be available instantly to surge in response to urgent current needs, so federal organizations must include planning factors that account for meeting long-range mission needs and unexpected surges in demand.

BSL-3 and BSL-4 laboratories contain special features to protect workers from potentially dangerous pathogens, and to prevent the release of infectious agents into the environment. Such design features include specialized ventilation systems to ensure directional airflow, air treatment systems to decontaminate or remove agents from exhaust air, controlled access zones, airlocks at laboratory entrances, or separate buildings or modules to isolate the laboratory.

In designing a high or maximum containment laboratory's physical features, the biological systems utilized to meet the agency's mission must be considered. For example, containment facilities required for agriculture research differ significantly from those needed to address human public health threats. Risk management for agriculture research is based on the potential economic impact of animal and plant morbidity and mortality, and the trade implications of disease that might result if infectious agents were inadvertently or intentionally released from containment. Containment strategies for working with large loose-housed animals or with plant crops, for example, result in different and sometimes highly unique additions and/or modifications to the typical BSL-3 and BSL-4 laboratories. These kinds of design differences impact the number and types of containment laboratories constructed.

Regardless of the unique requirements of specific BSL-3 and BSL4 laboratories, the need for an inclusive, highly skilled planning and design team is essential to ensure all critical design criteria have been included. For example, high and maximum containment laboratories supporting a homeland security or law enforcement mission require special attributes for evidence handling, processing, and forensic analysis that are unnecessary for a BSL-3 and BSL-4 laboratory engaged in vaccine or therapeutics development or study of an especially virulent plant pathogen. The underlying technical skill sets

necessary to plan, design, and oversee construction vary with the mission of the facility but are necessary across all projects. The unique mission-related requirements of each facility and the complex and comprehensive planning processes contribute to the protracted timelines necessary for construction of the high and maximum containment facilities.

Commissioning and verification testing are also requirements for high and maximum containment laboratories. Commissioning is the systematic review and documentation process confirming that specified laboratory structural components, systems and/or system components have been installed, inspected, functionally tested, and demonstrating that design criteria have been met. Many of these systems are highly complex and sophisticated. Commissioning is associated with the acceptance of the BSL-3 and BSL-4 laboratories from the contractor after construction or renovation and must be completed before the laboratory is used for its intended purpose. Characteristic of all high and maximum containment laboratories is the laboratory verification process (sometimes referred to as certification), which assures the routine and systematic examination of all safety features and processes within the laboratory (engineering controls, PPE, and administrative controls). Biosafety practices and procedures are also examined. It is an on-going quality and safety assurance activity that takes place on a regular basis that ensures that containment laboratories have:

- Proper engineering controls that are being used and are functioning properly as designed;
- Appropriate site and protocol specific administrative controls in place;
- PPE appropriate for the tasks being performed;
- Appropriate decontamination protocols and proper waste management procedures in place;
- Proper procedures for general laboratory safety, including physical, electrical, and chemical safety in place within the BSL-3 and BSL-4 containment laboratory; and
- Appropriately trained personnel.

In order to keep high and maximum containment laboratories operating as designed, highly skilled and trained operations, maintenance, and support staffs are necessary. The skills and knowledge required are unique to the systems necessary to meet the agency mission and are highly specialized.

These general characteristics of high and maximum containment laboratories contribute to the associated high construction, operating, and maintenance costs of these facilities, and to the long lead times that would be required to meet the demand for additional facilities. As a result, containment laboratory space cannot be developed in a timeframe

that will be responsive to any particular disease outbreak. For example, the Nation's ability to support the development of medical countermeasures applicable to the 2014 Ebola outbreak in West Africa has depended on decisions to develop high and maximum containment laboratory space that were made a decade ago or more. Similarly, decisions made today will influence the nation's capacity to conduct high or maximum containment research and respond to an emergency for many years to come.

Importance of High Containment Laboratory Work

Basic research on infectious agents and toxins and understanding the mechanisms by which they cause disease is fundamental to the Nation's ability to successfully counter biological threats, and combat disease. Research improves the detection, diagnosis, prevention, and response to biological agents. Research also yields new understanding of how microorganisms or their toxins function and cause disease, and how the immune system interacts with and defends against these infectious agents. Research provides a foundation for developing candidate vaccines against infectious agents, as well as therapeutics, and diagnostic tests that allow rapid detection of agents. Research laboratory infrastructure is critical to the protection of public health, agriculture, the environment, and homeland and national security.

Human health

Research in laboratory facilities has advanced the understanding and treatment of infectious diseases affecting humans, and has enhanced the ability to diagnose, treat, and prevent these diseases. Remarkable progress has been made to meet the challenges posed by infectious diseases such as Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS), tuberculosis (TB), influenza, plague, severe acute respiratory syndrome (SARS), and dengue fever. As an example, research has provided the scientific foundation for strategies to treat and prevent HIV/AIDS including combination antiretroviral therapy, post-exposure prophylaxis, and prevention of mother-to-child transmission. The recent Ebola virus disease outbreak is a reminder of the global threat of emerging infectious diseases and the continued need to support research that is responsive to new public health concerns. It also points to the benefit of having made prior investments in medical countermeasure research that can rapidly be adapted to urgent need. The public health crisis in West Africa requires concerted action, and speaks to the need to develop improved diagnostics, as well as safe and effective therapeutics and vaccines.

Agriculture

The introduction of animal and plant diseases to farms and pathogens to the food supply could cause severe public health and economic concerns. Research enables progress to

counter biological agent impacts on agriculture and the economy. To counter biological threats to agriculture, research in high containment facilities (equivalent to BSL-3) on livestock and crop pathogens, including high-consequence animal disease pathogenic microbes (e.g., foot-and-mouth disease virus and Avian influenza virus H5N1 virus), plant pathogenic microbes, pests, and invasive plant species, leads to improved approaches to protect U.S. agriculture and the food supply.[41] BSL-3Ag is used for studies involving large animals, especially when aerosol type pathogens are involved. As an example, research has provided the scientific foundation for the development of a vaccine to prevent Rinderpest virus, a deadly cattle plague that has led to devastating effects on agriculture. The result was the worldwide eradication of Rinderpest virus in 2011, which represents only the second time a disease has been eradicated in nature. [42]

Homeland and National Security

The need for strategies and products to protect public health and agriculture in the event of a bioterrorism event has resulted in the growth of biodefense research programs supported by the Federal Government that include research and related activities such as infrastructure development, training, and biosecurity measures. A biodefense infrastructure greatly enhances our ability to safely and efficiently conduct research on infectious agents.[43]

The focus of the U.S. biodefense enterprise is on the identification of harmful pathogens and outbreaks of infectious diseases and their containment, treatment, and elimination from the environment. These programs are managed by several departments and agencies with direct stakes in national security, environmental protection, and human, animal and plant health and safety, including the USDA, DOD, DOE, HHS, DHS, and the EPA. Research into infectious agents and toxins, including study of molecular mechanisms and related diagnostic, vaccine and therapeutic development, not only increases U.S. biodefense preparedness, but also offers inherent benefits for broader public health needs including the commercial development of enhanced technologies that support pathogen detection and medical intervention. Biodefense initiatives to improve human, animal and plant host defenses; to monitor emerging infectious diseases and drug-resistant microbes; and to clean up the site of a biological weapons attack have applications that benefit human, animal and plant health services, such as epidemiological disease surveillance and environmental remediation.

---

[41] The BSL-3 Ag maximum containment designation (equivalent to BSL-4) is used in large animal agricultural research only for zoonotic agents that can infect both animals and humans.

[42] For more information about research on emerging and re-emerging infectious diseases, see http://www.niaid.nih.gov/topics/emerging/pages/default.aspx.

[43] Testimony. NIH Implementation of Project BioShield in the Research and Development of Defense Countermeasures. July 14, 2005.

The biodefense infrastructure and its key resources, the laboratories, are essential to national security, public health and safety, and maintaining public confidence in our ability to prepare for and respond to emerging or re-emerging infectious diseases or deliberate attacks. Looking to the future, the U.S. biodefense infrastructure will continue to be a valuable national resource for developing measures to protect public health and agriculture against biological threats, whether due to natural causes or deliberate release. If adequately maintained, this infrastructure will continue to be a high national security priority for the foreseeable future.

Research Missions Requiring High-Containment Laboratory Space and Alignment of Containment Type with Mission

Different research missions require high-containment laboratories for the conduct of research. Examples of missions requiring high-containment laboratory space include:

- Basic Research. Basic research is critical to efforts to develop interventions against infectious agents and toxins. Basic research lays the groundwork by generating new and innovative concepts based on studies of pathogen biology and host response, and provides generalizable knowledge essential to understanding microbial pathogenesis and virulence.

- Applied Research and Countermeasure Advanced Development. Applied research builds on basic research by validating concepts in model systems and testing them in practical research settings. Successful medical countermeasure candidates (e.g., vaccines, diagnostics, and therapeutics) move into advanced product development, where they are manufactured and evaluated for safety and efficacy in animals, plants and humans according to strict guidelines and regulations.

- Attribution. Attribution is the collection of samples, and the conduct of forensic analysis, and characterization of the biological agents and toxins, and/or other material evidence associated with the biological event necessary for identifying the perpetrator of a deliberate attack. Attribution efforts may also include characterization and modeling of pathogen delivery or dispersal methods and associated systems or devices, and may address inclusion/exclusion of the potential biological source materials or agents used in the attack, to enable further investigations and analysis to help link people, places, things, and events.

- Emergency Response/Laboratory Surge. Readiness and surge capacity necessary to respond to naturally occurring infectious disease outbreaks, as well as to the accidental or deliberate exposure to biological agents are critical to our Nation's preparedness and response capabilities. For example, the Laboratory Response Network (LRN) was established by the CDC with the mission to "develop, maintain and strengthen an integrated domestic and international network of laboratories to respond quickly to biological, chemical, and radiological threats and other high priority public health emergencies needs through training, rapid testing, timely notification and secure messaging of laboratory results."[44]

Unique Experimental Capabilities and Design Features of High Containment Laboratories

In the United States, high containment laboratories are built to performance specifications that comply with funding agency design requirements and that incorporate at a minimum the design guidance provided in the *BMBL*. Depending on the research or production protocols planned for the space and the outcomes of site and protocol specific risk assessments, the design may also incorporate specific features required to support the research and/or production activities to be undertaken.[45] For example, BSL-3 laboratory design may need to incorporate sufficient space and configuration to support the use of biosafety cabinets housing flow cytometers, aerosolization chambers, sonicators and other aerosol producing equipment. High containment insectaries will incorporate design features unique to the work conducted with insects that ABSL-3 containment vivaria may not incorporate, including the use of nets, door sweeps, drain openings covered with approved stainless steel screens, closed sink valves and the absence of floor drains. ABSL-3 containment suites, which can house multiple and diverse configurations of adjoining holding and procedure rooms, may differ among institutions in the design of the air handling management systems needed to achieve the required negative directional air flow relative to the surrounding space. Depending on a risk assessment, inclusive of consideration of the air handling system design, ABSL-3 spaces in which aerosol-producing experiments with aerosol transmissible pathogens that are conducted outside of a biosafety cabinet may not be appropriate for co-location with ABSL-3 spaces used to support studies with agents that are not aerosol transmissible.

[44] Additional information about the LRN is available at: http://www.bt.cdc.gov/lrn/.
[45] For example, NIH published the NIH Design Requirements Manual (DRM), which outlines design requirements and guidance for biomedical research laboratory and animal research facilities in the U.S., including that for BLS-3 containment. More information on the DRM is available at: http://orf.od.nih.gov/PoliciesAndGuidelines/BiomedicalandAnimalResearchFacilitiesDesignPoliciesandGuidelines/Pages/DesignRequirementsManualPDF.aspx.

BSL-3 containment vivaria designed for studies involving large animals (BSL3-Ag) are specifically designed to protect the environment by including almost all of BSL-4 design requirements as enhancements that are not available in ABSL-3 vivaria; these include, but are not limited to, strict use of shower-out facilities, airlocks, fumigation chambers, large animal restraining devices, liquid effluent decontamination systems, and dedicated interlocked single pass, directional pressure gradient air handling systems that are High-Efficiency Particulate Air (HEPA) filtered on both the supply and exhaust lines. Similarly, enhanced BSL-3 suites incorporating some of the features described above are indicated for certain experiments involving HPAI viruses and other pathogens, as required by federal regulations and guidelines. Containment greenhouses supporting BL3-P research require additional safety considerations unique to work with invasive plants and plant pathogens and pests and the application of laboratory biosecurity.

In conclusion, the design requirements for high containment laboratories are determined by the work to be performed in them. Many of these spaces cannot be re-purposed to support other high containment work without renovation or adaptation based on research need. The appropriate sharing or re-purposing of high containment laboratories may be determined through site and protocol specific risk assessment only.

Previous Assessments of the Need for High-Containment Laboratories

Numerous reports, legislation, and Presidential Directives have addressed a national need to construct new or expand upon or replace existing biocontainment facilities. In February 2002, the National Institute for Allergy and Infectious Diseases (NIAID) at the NIH convened a Blue Ribbon panel on Bioterrorism and its Implications for Medical Research. In the ensuing publication, *NIAID Biodefense Research Agenda for CDC Category A Agents*, which articulates the panel's expertise, NIAID concluded that "[a]ccess to biosafety level (BSL) 3/4 facilities, particularly those with the capacity for animal model and clinical research, is limited and must be expanded."[46]

The 2002 Institute of Medicine report, *Biological Threats and Terrorism: Assessing the Science and Response Capabilities: Workshop Summary* [ISBN: 0-309-51025-2], noted that "Funding for basic scientific research, as well as for research associated with the development of new vaccines and therapeutics, must extend beyond the actual experimental work. Discussants noted that in order to accommodate the increased need for safely contained laboratory facilities, where some of this research must be conducted,

[46] *NIAID Biodefense Research Agenda for CDC Category A Agents,* February 2002, p. 4. , HHS/NIH/NIAID, See: https://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/biotresearchagenda.pdf.

laboratory capacity needs to be expanded. One possibility is the construction of new BSL-3 or BSL-4 laboratories and animal facilities in order to validate new vaccines and therapeutics…"[47] The report further noted that "scaling up research and development of all of these various potential therapeutics will require an evaluation of the availability of and need for additional laboratory capacity. In particular, there are a very limited number of BSL-3 and BSL-4 laboratories where nonhuman primate studies can be conducted."[48] NIAID/NIH and ASM conducted a survey in 2004 of academic, biotechnology, and pharmaceutical (non-federal) entities to address the location, capacity, and status of existing and operating BSL-3 laboratory facilities within the United States.[49] NIAID used the information garnered from the survey as an important part of the planning process for construction of new facilities. In November 2009, the Administration published the *National Strategy for Countering Biological Threats*,[50] which articulates priorities for domestic and international efforts to counter biological threats. In 2012, the National Research Council's Committee on an Analysis of the Requirements and Alternatives for Foreign Animal and Zoonotic Disease Research and Diagnostic Laboratory Capabilities published its report, *Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options*.[51]

Collectively, these reports, legislation, and Presidential Directives demonstrate the importance of ensuring that resources and infrastructure are available to meet the need to work with infectious agents and toxins. Examples of assessments addressing the need for high and maximum containment laboratories are noted in Appendix E. These assessments are based on research, development, testing, and evaluation needs that are conducted in support of national public health, agricultural health, homeland and national security, and biodefense needs.

Approach by which Departments and Agencies Evaluate and Develop Plans to Meet their Need for High and Maximum Containment Laboratory Space

---

[47] *Biological Threats and Terrorism: Assessing the Science and Response Capabilities: Workshop Summary* [ISBN: 0-309-51025-2], Institute of Medicine, 2002, page 10

[48] *Biological Threats and Terrorism: Assessing the Science and Response Capabilities: Workshop Summary* [ISBN: 0-309-51025-2], Institute of Medicine, 2002, page 114

[49] The *Survey for Determining the Location, Capacity, and Status of Existing and Operating BSL-3 Laboratory Facilities within the United States*, published in 2005, is available at https://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/bsl3_survey.pdf.

[50] Additional information about the *National Strategy for Countering Biological Threats* is available at http://www.whitehouse.gov/the-press-office/president-obama-releases-national-strategy-countering-biological-threats.

[51] *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, National Research Council. 2012

Departments and agencies in the Federal Government that require the use of high and maximum containment research laboratories to meet mission requirements conduct an extensive, complex, multi-year process to provide the capacity to meet those needs. The construction or renovation of laboratories should address future infrastructure needs for high and maximum containment facilities as well as the need for responsible stewardship of past investments in these containment facilities. Appendix F provides historical documentation for the establishment of the National Bio- and Agro-Defense Facility (NBAF). The historical documentation in Appendix F demonstrates the complex, multi-year process to establish a laboratory facility. Given the length of time necessary to establish a facility, decisions made years ago influence the nation's future capacity to conduct high or maximum containment research.

Federal departments and agencies have established priority and strategic planning processes to meet mission requirements, including the development and maintenance of infrastructure and facilities required to meet those needs. The priority setting and strategic planning processes includes extensive discussion and incorporation of input from a variety of sources, including Congress, the Administration, other federal agencies, scientific societies, the scientific community, patient groups, community advisory boards, public interest groups, and the pharmaceutical industry. As a result of the strategic planning process, and to meet the goals of federal department or agency programs, a need for additional high containment infrastructure is identified. Federal departments and agencies develop a budget request to meet mission requirements, which includes an annual performance plan describing goals for the requested funds and a performance report of how the previous year's goals were met. The department submits the request to the Office of Management and Budget (OMB), which reports to the President. OMB works closely with federal departments and agencies to create the budget that the President proposes to Congress. If the funds are included in the President's budget and appropriated by Congress, OMB apportions them to the requesting to the department, which can award construction funds for the structure, operations support, or refurbishment of these necessary biocontainment facilities. With their construction or renovation, USG programs are established or expanded intramurally or extramurally to meet mission requirements.

Common Processes

Collaborative mechanisms exist by which USG departments and agencies provide research capacity to each other, or work together to develop it. For example, the "Work for Others" program makes the national security biocontainment capabilities of DHS' National Biodefense Analysis and Countermeasures Center (NBACC) more broadly available to other federal agencies. Another example of federal collaboration is the

National Interagency Confederation for Biological Research (NICBR), a biotechnology and biodefense partnership and collaborative environment of seven U.S. Federal Government agencies at Fort Detrick, Maryland. In addition to NBACC, other biocontainment laboratories in the NICBR include the NIAID Integrated Research Facility (IRF), Naval Medical Research Center, USDA - Agricultural Research Services (USDA-ARS), National Cancer Institute Campus at Frederick (NCI-Frederick), FDA, and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).

DHS' Plum Island Animal Disease Center (PIADC) convenes a PIADC Senior Leadership Group (SLG) to provide an interagency forum for coordination of use of PIADC by DHS and USDA (both the ARS and Animal Plant Health Inspection Service [APHIS]) to allow both agencies to efficiently utilize the lab's unique capabilities to accomplish their respective mission-directed requirements. The SLG establishes operational (including security, safety, biosurety, health and environment) procedures and practices for PIADC and conducts strategic planning for future needs. A PIADC Board of Directors is responsible for coordination and oversight of all matters relating to the management, administration, research strategy and operations of PIADC.

USG Department and Agency Missions and Approaches to Determine High and Maximum Containment Facility Requirements

DOD

The DOD Chemical and Biological Defense Program's (CBDP) mission is to enable the U.S. military to deter, prevent, protect, mitigate, respond, and recover from chemical, biological, radiological, and nuclear (CBRN) threats.[52]

The CBDP provides medical and non-medical CBRN defense capabilities by providing a multi-layered set of protective measures to minimize chemical and biological warfare agent effects and by developing medical countermeasures in conformance with FDA licensure regulations and protocols.

The department establishes and maintains state-of-the-art research and test facilities and associated intellectual capital to foster world-class mission-critical research. As such, the Services' laboratories, university partnerships, international collaborations, and private sector laboratories performing CBRN defense-related activities must have the physical

[52] The 2014 DOD Chemical and Biological Defense Annual Report to Congress is available at: http://go.usa.gov/s8H9.

and intellectual infrastructure to provide products for the military service members and the United States.

High Containment Biological Facilities. Currently, the DOD operates several laboratories that possess, use, or transfer BSAT for biological defense research purposes. These laboratories perform the following functions to protect military service members from biological threats: (1) research to develop medical solutions—vaccines, drugs, diagnostics, and information; (2) non-medical defense acquisition from basic and applied research through technology development, engineering design, equipment evaluation, product support, sustainment, and demilitarization; (3) planning, conducting, and analyzing results of development and production tests; (4) non-medical Research, Development, Testing, and Evaluation (RDT&E) of agent detection, identification, and diagnostic systems; (5) non-medical RDT&E, systems engineering, and modeling and simulation to support development of protection, detection, and decontamination systems; and (6) research on and surveillance of a wide range of infectious diseases in support of deployed military forces.

Determination of needs for DOD research and development. DOD's need for laboratory capabilities and capacity are determined by its strategic priorities for the research and development of defensive systems to protect military service members from chemical and biological threats. Strategic priorities are revisited on an annual basis, informed by threat assessments, operational risk assessments, evaluation of existing programs, and the output of a strategic portfolio review. These inputs collectively contribute to program strategic guidance, issued by the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs, which guides CBDP component planning and programming decisions, to include the direction and magnitude of DOD's research and development activities. In turn, these decisions determine the scope of DOD's needs for laboratory capability and capacity.

DOD evaluation of need for an animal test and evaluation facility. To address the escalating need for U.S. biodefense capabilities, the Executive Office of the President and DOD issued executive strategies and directives aimed at enabling the nation to prepare for, respond to, and minimize the consequences of a biological attack. A White House Memorandum (Medical Countermeasures Against Biological and Other Public Health Threats, December 29, 2010) tasked the Secretary of Defense to "establish a Medical Countermeasure (MCM)-Test and Evaluation (T&E) Facility to provide state-of-the-art capacity and services to address the national demand for animal T&E studies and related requirements for product development."

In 2012, the U.S. Army completed a requirements study to forecast the demand for a BSL-3 and BSL-4 animal T&E laboratory. The study assessed the existing capacity

within Government, industry, and academic laboratories to support this demand. Based on the findings of the study and of expected throughput of new medical countermeasures, the U.S. Army intends to utilize current facilities and the new USAMRIID that is under construction to meet its needs for testing and evaluation of MCM in ABSL-3 and ABSL-4 laboratories.

In conclusion, the DOD CBDP supports research programs based in DOD Service laboratories to ensure preservation of scientific expertise, intellectual critical mass, and infrastructure while concurrently maintaining an appropriately balanced investment portfolio across all external coordination activities. It manages defense programs from basic research through procurement and sustainment. These research, development, and acquisition programs will provide U.S. forces with the best equipment and medical products to ensure their survivability and mission accomplishment on any future battlefield where biological (or chemical) agents may be employed.

DHS, Science &Technology (S&T) Directorate

The mission of the DHS is to secure the nation from the many threats faced and to keep America safe. Critical to protecting this nation against diseases are biological laboratories.

PIADC. Since 1954, the PIADC, just off Long Island, New York, has served as the front line of the nation's defense against diseases that could devastate markets for livestock, meat, milk, and other animal products. The PIADC celebrated 60 years of operation in the summer of 2014. USDA and DHS conduct research at PIADC. USDA ARS provides research services on high-consequence foreign animal diseases (FADs) and develops diagnostic tools, vaccines, and other means for preventing FADs. USDA APHIS activities at PIADC provide FAD diagnostic services for the nation; PIADC is the only laboratory in the nation that can conduct initial diagnostic testing for foot-and-mouth disease. APHIS also develops novel diagnostic tools and maintains the North American Foot and Mouth Disease Vaccine Bank. Also, APHIS conducts training for federal and state veterinarians who serve as the first responders in a potential outbreak of a foreign animal disease. The Transboundary Animal Disease Countermeasure Development Branch at PIADC, part of the DHS S&T Directorate, takes vaccines developed by ARS, academia, and/or private industry through the regulatory process for licensing new vaccines and diagnostics for high-threat FADs.

NBAF. The NBAF, currently under construction in Manhattan, Kansas, will be a state-of-the-art BSL-3, BSL-3Ag, and BSL-4 facility that will enable the United States to conduct comprehensive research, develop vaccines and anti-viral drugs, and provide enhanced

diagnostic capabilities to protect our country from foreign animal, emerging and zoonotic diseases. As a replacement to the PIADC, NBAF will provide additional capabilities that are not currently available in the United States including BSL-4 space for large livestock and a biotechnology development module (e.g., master seed production). The NBAF Central Utility Plant (CUP) construction contract was awarded in February 2013 and is at 65 percent completion; main laboratory construction is planned to start in May 2015. Current operations at PIADC will continue through NBAF construction. DHS and USDA (ARS and APHIS) are developing a transition plan from PIADC to NBAF that includes an overlap of operations to ensure there is no interruption of the critical science missions.

NBACC. The NBACC, located at Fort Detrick in Frederick, Maryland, is the first national laboratory created by DHS. NBACC's mission is to provide the scientific basis for the characterization of biological threats and bioforensic analysis to support attribution of their planned or actual use. NBACC components include the National Bioforensic Analysis Center and the National Biological Threat Characterization Center. NBACC has unique national BSL-3 and BSL-4 aerobiology capabilities, which are required to obtain key scientific data that informs biodefense planning and response. NBACC provides more than 50,000 square feet of BSL-2, 3, and 4 laboratories including continuous operational support to law enforcement.

DHS S&T Directorate's extramural programs (based on critical homeland security mission requirements) that require biocontainment facilities come from the Homeland Security Advanced Research Projects Agency which included the Chemical and Biological Defense Division (CBD), PIADC and NBACC sub-contracts, Cooperative Research and Development Agreements, Interagency Agreements (IAAs), etc., as well as the Office of University Programs (OUP) that engages the academic community to conduct research and analysis, and provide education and training to enhance the department's homeland security capabilities. OUP offers a variety of vehicles through which DHS components and other partners can access the research and expertise found at the DHS S&T Centers of Excellence (COE):

1. Basic Ordering Agreements (BOAs) - Through a BOA, DHS components can establish a contractual task order directly with a COE to conduct targeted research and development or education projects.

2. Cooperative Agreements and Grants - OUP has a suite of standing cooperative agreements and grants with dozens of colleges and universities. DHS components and other federal agencies can tap into these vehicles through a variety of partnership opportunities or IAAs with OUP.

OUP currently funds nine COEs (each focused on a unique homeland security need) with two COE working on DHS-funded projects requiring biocontainment facilities:

- National Center for Zoonotic & Animal Disease Defense: Kansas State University and Texas A&M University - protects the Nation's agriculture and public health sectors against high-consequence foreign animal, emerging, and zoonotic disease threats.
- National Center for Food Protection & Defense: University of Minnesota - defends the safety and security of the food system by conducting research to protect vulnerabilities in the Nation's food supply chain.

HHS/NIH/NIAID

The terrorist attacks of September 11, 2001, followed by *B. anthracis* mailings in October of the same year made clear that terrorism represents a serious threat to our Nation and the world. These events resulted in considerable deliberation and a thorough reassessment of our national preparedness for deliberate biological attacks, as well as for high-consequence infectious diseases that could compromise our public healthcare system. In February 2002, NIAID convened a Blue Ribbon Panel of independent experts to consider specific actions that could be taken to fulfill its dual mission – to anticipate and respond to bioterrorism and to address endemic and emerging diseases. The recommendations of the panel led to *NIAID's Strategic Plan for Biodefense Research* and to the development of an extensive and detailed research agenda for Category A, B, and C priority pathogens.[53] Specifically, the panel identified the lack of secure and appropriately designed laboratories as a major gap in our national capability to conduct research on, and develop medical interventions for, pathogens that can cause severe disease via an inhalational route of exposure.

Extramural Biocontainment Laboratories. In 2003, Congress authorized ~$375 M for construction of extramural biocontainment laboratories to address the critical shortage of such facilities, leading to the establishment of two National Biocontainment Laboratory/ BSL-4 facilities (University of Texas Medical Branch and Boston University) and twelve Regional Biocontainment Laboratory BSL-3 facilities. These state-of-the-art facilities were viewed as a necessary commitment in order to support the panel's broad research agenda recommendations, and were intended to function in concert with NIAID's extramural Regional Centers of Excellence. The design and implementation of these

[53] Information about Category A, B, and C pathogens is available at: http://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx

laboratories was done in a collaborative and transparent manner, integrating the specialized expertise and agreement of academic, government and public sectors.

Intramural Biocontainment Laboratories. The NIAID Strategic Plan called for an expansion of NIAID's basic and translational research capabilities on bioterrorism agents. This led to the incorporation of funding by Congress in the 2003 NIH budget for the construction of three high containment research facilities for the NIAID intramural research program: the C.W. Bill Young Center for Biodefense and Emerging Infectious Diseases in Bethesda (BSL-3), the Integrated Research Facility at the Rocky Mountain Labs in Montana (BSL-4), and the Integrated Research Facility at Fort Detrick (BSL-4). As a result of these directives, the NIAID mission has expanded with a major focus on biodefense as well as emerging infectious diseases, which share some of the same hazards and risks to public health as bioterrorism agents. For the planning and design of each of the three high containment research facilities constructed by the NIAID intramural research program, NIAID management convened expert technical and scientific advisory panels. These panels along with NIH and NIAID leadership developed a program of requirements for each facility. As part of this process and the previous deliberation of the Blue Ribbon Panel, several factors were evaluated to determine the amount of space required for BSL-3 and BSL-4 research.

Factors included:

- The number of different scientific programs that were planned for each building. For example, the C.W. Bill Young Center for Biodefense and Emerging Infectious Diseases had eight different scientific programs or laboratories (respiratory viruses, poxviruses, viral hemorrhagic fevers, etc.) that were planned as critical components to the biodefense mission. The eight programs were further subdivided into sections for determination of staffing and space requirements. These eight programs were then assigned an estimated footprint of BSL-2 and BSL-3 laboratory and vivarium space ranging from 5,000 to 8,000 net assignable square feet. Likewise, core functions such as imaging or flow cytometry were allocated space.
- The extensive list of biodefense agents and emerging infectious disease agents that were determined to be priority pathogens for investigation. NIAID was charged with developing or expanding significant research programs on numerous pathogens. The Category A, B, and C Pathogen List developed by NIAID and other U.S. Government agencies prompted study of diverse bacterial and viral agents requiring a large expansion of high containment space. NIAID had no BSL-4 capability and very limited BSL-3 space to perform research on these pathogens prior to 2001.

- Required separation of research on select pathogens for biosafety or biosecurity. For example, certain influenza strains should not be co-located in order to prevent the accidental exchange of genetic elements that might increase virulence. Additionaly, work with some agents required unique vaccination or PPE procedures. Based on biological risk assessment, study in isolated laboratories was warranted to decrease risk to research staff.
- The NIAID mission for research on these biodefense agents was broad. NIAID identified four major research areas to pursue on each pathogen of concern; vaccines, therapeutics, diagnostics, and basic research. This broad directive, in some cases, resulted in a need for multiple high containment suites for select pathogens because of the large volume of research and staffing.

Similar to the construction of extramural high containment laboratories across the United States, NIAID undertook intramural facilities construction based on the projected programmatic needs for ongoing and expanded intramural research in biodefense and emerging infectious diseases.

Biodefense Research. A significant component of NIAID's biodefense mission has involved the development of animal models of disease for biological threat agents, and the evaluation of countermeasures in these models. The Blue Ribbon Panel underscored the importance of expanding non-human primate testing capacity for potential vaccines and therapeutic candidates, all of which must be done under BSL-3 or BSL-4 conditions. Thus, a major planning consideration for biocontainment laboratory space has been to accommodate this need, and to do so in concert with interagency partners (e.g., DOD, FDA, and DHS) whose expertise and guidance was essential to satisfy the technical and statutory requirements for such studies. The priorities for studies of bioterrorism agents have been driven largely by material threat assessments and thus represent the consensus views of our Government partners (i.e., Public Health Emergency Medical Countermeasures Enterprise [PHEMCE]) that have overlapping biodefense missions.

Public Health Research. The public health research agenda of NIH is less prescribed than that of biodefense, and the facilities needed to support this mission have been based on the historical priorities of infectious disease (e.g., influenza, TB), as well as by zoonotic and emerging diseases. This process has involved ongoing communication with the veterinary community (including USDA) to identify diseases with the potential to emerge in humans. As with biodefense research, animal models are often required to fully understand disease pathology and develop appropriate disease treatments, requiring BSL-3 containment at a minimum. The priorities for public health are difficult to predict, and may change rapidly (e.g., SARS, H5N1 influenza, Chikungunya, Ebola, etc.). Therefore, it was important to anticipate future needs by planning new facilities that

could respond to evolving public health concerns. Laboratory space was designed to retain flexibility and ensure that the extramural community could carry out the basic research needed to address emerging diseases. The design, construction and certification of biocontainment laboratories require long lead times, and our Nation made the commitment to build an infrastructure that is capable of responding to unforeseen disease scenarios.

The need for high containment space was projected based on broad assessments of experimental efforts that would accompany the expansion of extramural research that was authorized in 2003. It was recognized that no single "module" of containment space could support all needs, and that different configurations would be needed, depending on the objectives of the studies, e.g., animal models for disease, basic research on communicable diseases, and evaluation of tissues infected with transmissible agents. In addition, changes in pathogen-related research priorities and regulatory requirements could impact the amount of space required and how it might be used. Thus, due to the complexity and diversity of anticipated research, the planning was designed to create sufficient containment space to address many potential needs, while ensuring that investigators would have minimal risk of exposure to harmful pathogens.

The use of NIAID high containment facilities requires both external approval of the research, via a peer-reviewed process of funding for scientific merit, as well as a subsequent process that evaluates the performance of efforts by extramural staff. All NIAID-supported biocontainment facilities must adhere to strict regulatory and security guidelines that are monitored by facility staff at those sites and periodic assessments by external committees are made to ensure that the operation of these facilities meets institutional standards.

USDA

An overview of USDA's mission and decision-making process for developing, maintaining and modernizing USDA high containment facilities follows.

USDA Plant High Containment Facilities. The USDA ARS Foreign Disease and Weed Science Research Unit (FDWSRU) has two distinct missions united by a common relationship to plant pathology and the unit's unique high containment plant pathogen laboratory and greenhouse containment facilities. The USDA ARS FDWSRU is located at Fort Detrick in Maryland. ARS scientists research foreign plant pathogens that have not been introduced in the United States but pose a potential threat to American agriculture. This ARS program utilizes several buildings on the Fort Detrick site that include labs, offices, greenhouses and a BL-3 enhanced high containment facility that

contains small labs, growth and dew chambers and greenhouses. Originally built in the mid-1950s, the facility went under its first renovation in the mid-1980s and is currently in the middle of a second renovation. The research on high consequence plant pathogens conducted by FDWSRU focuses on increasing understanding of their biology, vector transmission, host range, and molecular characterization. These pathogens are also used for the development of diagnostic assays and the preservation of index cases of exotic isolates of plant pathogens. In addition, the FDWSRU has a program for evaluating technology for weed control. This ARS group works closely with the USDA APHIS Plant Protection and Quarantine (PPQ) laboratory in Beltsville, Maryland.

The USDA APHIS PPQ program conducts applied research in this facility in conjunction with scientists from USDA ARS and United States and international academic institutions to adapt and validate diagnostic test methods for screening and confirmatory testing. The PPQ high containment laboratory and greenhouse, located on the USDA ARS Beltsville Agricultural Research Center campus in Beltsville, MD, is certified BL-3. It was constructed in the late-1990s through early-2000s and was occupied in 2005. The APHIS space contains one laboratory, four specialized growth rooms, and a large containment greenhouse divided into 10 smaller sections to accommodate work on diverse high consequence plant pathogens. APHIS PPQ in Beltsville, Maryland is the reference and confirmatory testing laboratory for diagnostic testing of plant pathogen incursions into the United States or plant pathogens detected in national surveys, emergency programs or pathogens sent from Plant Inspection Stations or Ports of Entry. Similar to APHIS Veterinary Services (VS), APHIS PPQ is involved in the work of the National Institute of Food and agriculture diagnostic efforts of the National Plant Diagnostic Network (NPDN) which is the plant pathogen counterpart to National Animal Health Laboratory Network (NAHLN). APHIS PPQ provides hands-on laboratory training in-house at the facility and also provides the NPDN with diagnostic protocols for regulatory plant pathogens which are the focus of national surveys or eradication programs. At this facility, plant pathogens that are detected in new U.S. incursions are isolated and preserved for diagnostic test development, validation or biological evaluation; they may be transferred to other USDA ARS high containment facilities for longer-term preservation and storage. The PPQ high containment facility is used to develop a limited number of proficiency test panels of high consequence regulatory plant pathogens as part of the APHIS PPQ National Plant Protection Laboratory Accreditation Program, which authorizes laboratories and analysts to perform screening diagnostics for PPQ pathogens and pests. This facility is also used to train inspectors from APHIS PPQ and the FSAP and develop skills required to conduct inspections of high containment and registered select agent pathogen facilities.

USDA Animal High Containment Facilities. ARS currently has three high containment laboratories: 1) National Animal Disease Center (NADC), located at the National Centers for Animal Health in Ames, IA, 2) Foreign Animal Disease Research Unit (FADRU), co-located with APHIS and DHS laboratories at PIADC, Orient Point, New York, and 3) the Southeast Poultry Research Laboratory (SEPRL) located in Athens, GA. All three laboratories include BSL-3 and ABSL-3 laboratory space to work on poultry and NADC and FADRU additionally have BSL-3Ag animal facilities to work on large animals, including wildlife.

The ARS mission has unique and critical resources dedicated to ensuring that agricultural production is secure, sustainable, and efficient with the aim of providing healthy, safe, and affordable food. Because many high consequence pathogens have the potential to spread across national borders, ARS must maintain the ability to conduct research on diseases that threaten animal and plant or public health. As a result, ARS has developed and maintained a number of high-containment laboratories capable of conducting research on foreign and zoonotic pathogens. ARS has implemented an agency wide facility modernization program involving major facility upgrades at high priority research locations selected by the Administrator and the National Program Staff. These modernization sites are selected and prioritized based on criteria which include high priority programs; safety and health of employees; a critical mass of scientists; and established centers of excellence for high priority research programs. Development of facilities is based on ARS specific agency policy manuals: ARS 242.1 *ARS Facilities Design Standards* and ARS 242.5 *Economic Analysis and Decision for ARS Facility Modernization*. The entire physical containment system for ARS high containment facilities must function to prevent the spread of infectious agents to the environment, to other animals or plants, and between research experiments, as well as to humans.

The National Centers for Animal Health. The National Centers for Animal Health is a recently upgraded campus in Ames, Iowa comprised of three separate USDA entities: the ARS-National Animal Disease Center (NADC), the APHIS-National Veterinary Services Laboratories (NVSL), and the APHIS-Center for Veterinary Biologics (CVB). The facilities for all three entities have been consolidated and the combined campus is called the National Centers for Animal Health. However, NADC, NVSL and CVB each retain their separate identities, reporting structure to their respective agencies, and missions. The three centers operate a team of combined support services that provide various support activities (engineering, animal care, information technology, warehouse, shipping and receiving, and laboratory services) to the entire campus. The NADC, NVSL, and CVB are critical and indispensable national resources for our animal health care delivery system.

The NADC is the major USDA center for research on livestock and poultry diseases that occur in the United States. It was first constructed in 1961 and totally renovated and modernized in 2009. It is one of the world's largest animal health research facilities. Its mission is to conduct basic and applied research on priority endemic and emerging zoonotic animal diseases as well as food safety concerns of major economic importance to the U.S. livestock and poultry industries. The goal of its research programs is to solve problems of high national priority with a focus on preventing and controlling animal diseases by generating knowledge and technologies to reduce economic losses associated with production diseases and mitigate the threat of zoonotic diseases on public health. Priority zoonotic diseases include emerging swine influenza viruses, brucellosis, TB, and leptospirosis.

APHIS' NVSL is the reference and confirmatory testing laboratory for USDA. It consists of three laboratories at Ames, Iowa, in the USDA National Centers for Animal Health, and one laboratory located in the DHS's PIADC. In 2009, NVSL moved into shared facilities with the ARS at Ames. The APHIS CVB, which conducts laboratory testing for its biologic regulatory program, also moved into the new facilities in 2009. The laboratory space, including BSL-2 and BSL3, was designed to handle current program testing and provide additional space for the Diagnostic Virology Laboratory that had been in compacted space. The NVSL laboratory at the PIADC and the Foreign Animal Disease Diagnostic Laboratory will be moving into approximately the same amount of space it currently occupies when DHS completes construction of the NBAF in Manhattan, Kansas.

To assist in meeting the surveillance and surge capacity needed for animal health programs and foreign animal disease detection, USDA APHIS coordinates with the National Institute of Food and Agriculture and the American Association of Veterinary Laboratory Diagnosticians, to support NAHLN. The NAHLN consists of 60 laboratories operated by universities or state animal health departments that conduct specific, specialized testing on behalf of the Federal Government. The Federal Government is in the process of making proposed changes to the NAHLN structure. The proposed changes includes determining core NAHLN laboratories based on factors such as geography, animal distribution, commodity demographics, farm gate values, pathway/risk assessment and capacity. The NAHLN laboratories were not constructed to meet federal testing needs, but to respond to private needs of producers and the livestock industries and receive some level of state support.

For APHIS, capacity is considered to be the number of samples that can be tested during normal outbreaks and recovery periods for a disease, plus the capacity to confirm disease identification in the case of foreign or emerging diseases. Included in the consideration

for capacity are: the impact of disease on trade and economy should an outbreak occur in the U.S., whether APHIS Veterinary Services has an active eradication/management program for the disease, overall impact to public health, current capacity of other laboratories to diagnose the disease, and current availability of biologics or vaccines to treat the diseases in animals. APHIS also requires large animal biocontainment facilities as part of their mission as an emergency response agency for when it is necessary to perform diagnostic or product evaluation procedures in live animals in BSL-3 enhanced (Ag) facilities within a 24 hour notice for potential emerging or foreign animal disease incursion.

The Food Safety and Inspection Service (FSIS) mission is to ensure that the nation's commercial supply of meat, poultry, and egg products is safe, wholesome, and correctly labeled and packaged. FSIS commissioned (and maintains) one, in-house BSL-3 laboratory to enhance capacity and capability through analytical testing of FSIS-regulated products. The role of this laboratory is to provide safe and secure in-house laboratory support for screening and limited confirmation of high risk agents on an as-needed basis. Surge capacity needs are estimated by agency risk assessments, FSIS compliance activities, and threat information or assessments from DHS. Backup surge capacity and capability to support the FSIS mission or recovery phases of food emergencies are available on local, regional or national levels. FSIS can expand analytical surge capacity and/or capability through extramural cooperative agreement funding provided to multiple state or local laboratories (Food Emergency Response Network). Capacity and capability estimates are evaluated during annual requalification queries of laboratory characteristics and through participation in proficiency testing and exercises. Annual queries also note laboratory involvement in other networks (food testing laboratories may be members of multiple emergency response networks) which could adversely impact the laboratory's ability to surge for food testing during a widespread food emergency.

FADRU. The ARS FADRU at the PIADC is operated by DHS and described elsewhere in this document.

SEPRL. Established in 1960, SEPRL is a world leader in developing research solutions to the most deadly poultry diseases such as HPAI and Newcastle disease, which have devastated poultry and wild bird populations around the world. This includes playing a key role in developing rapid genetic diagnostic tests and vaccines used to control these diseases, not only in United States but also globally. The national and international experience of the laboratory has resulted in it being designated a Collaborative Center on research on emerging avian diseases by the World Organization for Animal Health. The threat of H5N1 and H7N9 avian influenza or 'bird flu' has shown itself to be both a veterinary and a public health issue with poultry and zoonotic outbreaks highlighted in

the past few years with deaths in poultry and people in Asia, Africa, and Mexico. The SEPRL scientific program continues to play a key role in developing the next platform of vaccines against these diseases and new diagnostic tests that will keep these devastating diseases out of the United States. The SEPRL scientific expertise brings together an integrated research approach that includes virology, molecular biology, pathology, and immunology, which is key to developing prevention, management and control and eradication strategies that protect the $25 billion/year U.S poultry industry ($2.5 billion in U.S. exports). To effectively respond to the research needs of the United States, SEPRL requires new laboratory and animal housing facilities if it is to remain competitive and continue providing rapid responses to new and emerging disease threats.

Shared Responsibilities

Opportunities to share biocontainment space among USG departments and agencies based on common goals and responsibilities are a consideration for addressing the need for appropriate containment space in the United States. Optimization of resources and efficiencies can be attained through sharing of department and agency resources related to laboratory usage. For example, DHS and USDA are working collaboratively to establish the NBAF. As background, DHS is charged with the responsibility and has the national stewardship mandate for detecting, preventing, protecting against and responding to terrorist attacks within the United States. These DHS responsibilities as applied to the defense of agriculture are shared with the USDA, and require development of a coordinated strategy to protect the nation against biological threats to animal and plant sectors of agriculture. Consultations between DHS and USDA on a coordinated biodefense strategy, as called for in the Homeland Security Act of 2002, revealed a high containment infrastructure gap that had to be filled by an integrated RDT&E Biosafety Level (BSL) 2/3/3Ag/4 facility for combating bio- and agro-terrorism threats. The DHS S&T Directorate is responsible for filling the gap in biocontainment infrastructure as defined by the related homeland security efforts of DHS and USDA.

The Homeland Security Act of 2002 recognized that protection of U.S. agriculture is a critical element of homeland security and transferred ownership of PIADC from USDA to DHS in 2003. Recognizing the growing need for veterinary countermeasures to protect this Nation's agricultural sector and recognizing the limitations posed by the current facility to meet this requirement, Homeland Security Presidential Directive 9 (HSPD-9), *Defense of United States Agriculture and Food*, directs that the "Secretaries of Agriculture and Homeland Security will develop a plan to provide safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases." Furthermore, HSPD-9 requires that DHS, USDA and others "accelerate and expand development of current and

new countermeasures against the intentional introduction or natural occurrence of catastrophic animal, plant, and zoonotic diseases." The Secretary of Homeland Security is responsible for coordinating these activities.

The NBAF will be a state-of-the-art BSL-2/3/3Ag/4 facility located in Manhattan, Kansas, that will enable the United States to conduct comprehensive research, develop vaccines and anti-viral therapies, conduct training, and provide enhanced diagnostic capabilities to protect our country from foreign animal, emerging, and zoonotic diseases. NBAF will provide additional capabilities not currently available in the United States including BSL-4 space for livestock, and a biotechnology development module for master seed production (enhancing collaborations with animal health companies). DHS and USDA (ARS and APHIS) have worked collaboratively at PIADC to plan NBAF since January 2004 (joint milestones include the Expression of Interest for Potential Sites for NBAF published in FedBizOpps January 2006; NBAF Feasibility Study August 2007; Final NBAF Environmental Impact Statement December 2008; NBAF Schematic Design Completed November 2009; Site Specific Threat and Risk Assessment January 2010; Site-Specific Threat and Risk Assessment (SSRA) based on the 35% NBAF design documents issued October 2010; Updated SSRA February 2012; NBAF design completed July 2012; planning for the transition from PIADC to NBAF; etc.). See Appendix F for NBAF Program Requirements-Historical Documentation.

Identification of "Best Practices" for the Construction or Renovation of High Containment Laboratories

The establishment of best practices for the construction and maintenance of high and maximum containment facilities would support the responsible stewardship of investments in these facilities.

The Federal Government has available the *BMBL*, the *U.S. Department of Agriculture/ Agricultural Research Service (USDA/ARS) 242.1 ARS Facilities Design Standards*, the *World Health Organization (WHO) Biosafety Guidelines: Biosafety Manual*, and the *National Institutes of Health Design Requirements Manual* (*DRM*). These are viewed as minimum standards that are used by the Federal Government. The Federal Government relies on industry standards such as the International Building Code, Fire Code, Plumbing Code and Mechanical Code; the American Society of Heating, Refrigerating and Air Conditioning Engineers (ASHRAE) standards; and the American National Standards Institute (ANSI)/ American Society of Safety Engineers (ASSE) standard: *Testing and Performance-Verification Methodologies for Ventilation Systems for Biosafety Level 3 and Animal Biosafety Level 3 Facilities (ANSI/ASSE Z9.14)* . These documents when

used in conjunction with agency specific design criteria for high and maximum containment laboratories constitute best practices.

When a federal agency makes the final determination to expand its high and maximum containment facility research base, whether through a new facility, the modernization of an existing infrastructure, or a new mission-directed initiative requiring specific enhancements to an existing laboratory, facility design, construction and commissioning are of paramount importance. A well thought out strategy should include funding, procurement of design and construction services, realistic design and construction time-frames, and strong construction management oversight by the funding federal agency.

The funding strategy is critical to ensure completion of the process. Funding supports 1) planning, design and construction and 2) recurring expenses.

A funding package must include Architectural and Engineering (A/E) design consultation fees, A/E contract drawing fees, A/E construction management fees and inflation adjustments for the duration of the actual construction period.[54] These alone can represent 27%- 30% of appropriated funds over and above the estimated construction costs. Additionally, any funding strategy should include recurring costs such as maintenance contracts to sustain peak operational performance and recertification of the facility (or equipment); consideration for additional support staff; and utility expenses. Over time, the recurring costs will far exceed the cost of design and construction. If recurring costs are not factored in, the lack of ongoing financial support could result in a failure to meet the original intent and may necessitate a redesign or other unintended consequence.

Challenges are faced when an agency decides to renovate an existing laboratory containment for a purpose other than what it was originally designed for, such as converting a BSL-2 laboratory to a BSL-3 laboratory, retrofitting a laboratory to perform work with an aerosolized BSAT agent, or converting an existing space to a BSL-3Ag high containment laboratory. Entities wanting to enhance a laboratory for BSAT studies have had difficulty meeting the BSAT regulatory and biosafety requirements necessary to account for agent-specific characteristics. There is a new trend in which organizations are applying the concept of "swing space" which allows competing research companies to use generically designed high containment space to conduct studies. These well intended

[54] Specialized biocontainment requirements will influence funding if not accounted for in pre-design discussions and design development, such as constructing and validating prototype mock-up's for high-containment greenhouses, or the application of bio-bubble technology for use in large animal studies.

efforts could have substantial cost implications, especially if the space is not ideally suitable for improvement.

The federal procurement process for design and construction services is complex and involves obtaining the needed expertise specific to high and maximum containment facilities for the design and construction of these facilities. The Federal Government's contracting process[55] includes the Request for Proposal (RFP) process, which allows an agency to vet qualified design firms to reduce the likelihood of contracting with an inexperienced company, as well as establishing fixed rates for architecture and engineering (A/E) design consultation fees, design/development fees, and A/E construction management fees for the duration of the project.

In order for an agency to meet its desired implementation target, the design and construction process is held to a specific time-frame, usually with limited flexibility. Once the decision is made to proceed with the project, regardless of size and complexity, a realistic time-frame needs to be established. The request and acquisition of funds must always be linked to the implementation target date. This will ensure that sufficient funds are available to complete the project. For example, if funds are appropriated in 2015 and the planned implementation date is set for the end of 2017, then the appropriated funds should be able to carry the project through to the end of 2017.

Additional Factors Governing Need for High or Maximum Containment Laboratory Space

Each department and agency operating high or maximum containment laboratory space has established processes to determine how much BSL-3 or BSL-4 laboratory space it requires to address its mission. If each department/agency has appropriately considered all downsides, costs, or risks from building and operating containment lab space, and has weighed those costs appropriately against the benefits that these laboratories will provide in terms of fulfilling the department or agency mission, they collectively, will be positioned to build the nationally optimal amount of laboratory space. On the other hand, if the department or agency does not consider all risks that might accrue from the construction or operation of these laboratories - i.e., if it does not address concerns expressed by the community about the building of these laboratories; if it does not sufficiently commit to long-term maintenance and support; or if it does not include potential negative public perceptions in their analyses – the department or agency might

[55]The Federal Government's contracting process is generally governed by the Federal Acquisition Regulations (FAR) which stipulates acceptable contracting procedures.

build excess laboratory space, because it would be capturing the benefits of such research in its analyses but may not have captured all the risks.

Departments and agencies may also develop a suboptimal distribution of their various high-containment laboratories if they are not able to consider each other's activities when making plans. Although assessment of inter-agency capabilities has been a consideration in facilities planning in the past, a more formal process by which departments and agencies review each other's proposed plans for the construction or renovation of laboratories to meet infrastructure needs could create synergies and potentially reduce the total amount of laboratory space required. The establishment of a formal process could include the development of identified best practices for the construction or renovation of laboratories.

An objective assessment by a non-federal entity of federal department and agency efforts to ascertain the appropriate number of high containment facilities to possess, use, or transfer BSAT may assist in determining the appropriate number of high containment U.S. laboratories. An objective assessment of each department or agency's determined need for high containment laboratory space could help to ensure a consistent and uniform approach related to decision-making.

Challenges

Challenges exist related to the identification of the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT. These include:

- Definition of a Laboratory. Some high-containment laboratories are designated to operate only occasionally at the BSL-3 level – i.e., for particular experiments - depending on the protocol and associated risk assessments for those protocols. Most of the time, these facilities operate as BSL-2 laboratories, although they are designed to operate safely and securely at the BSL-3 level, as needed. Consideration must be given to how these transient BSL-3 facilities should be considered in the determination of the appropriate number of high containment U.S. laboratories capable of possessing, using, or transferring biological select agents and toxins.

- Unpredictability of the New Emergence or Re-emergence of Infectious Diseases. Laboratory containment needs change with time and may need to scale up rapidly during an infectious disease outbreak (e.g., Ebola virus disease). The specific biohazardous agents that emerge are not typically predictable, although it is certain that future infectious diseases outbreaks will occur thus making such space

necessary. The human population is expanding at an exponential rate; people are living in more densely crowded conditions in many parts of the world; and transportation systems are such that there is greater connectivity of populations that may be separated by great geographic distances; but are well within an interval of travel to be in contact within the incubation period of most infectious diseases. A 2014 report, based on an analysis of more than 12,000 outbreaks involving 44 million people during the last 33 years, identified a global rise in human infectious disease outbreaks around the world.[56] Flexible and expandable laboratory capacity and capability is necessary to address emerging threats and to ensure our Nation's preparedness for future outbreaks.

- Emergence of Technologies. The technologies available for scientific research are rapidly evolving. The development and use of attenuated virus models (e.g., reverse genetics or virus-like particle model systems) in the place of virulent fully intact viruses may enable the use of lower level biosafety level conditions (e.g., BSL-2 instead of BSL-3 or BSL-4) to advance understanding of the basic biology and pathogenesis of these high consequence pathogens. The wider application of molecular safety controls in viruses studied in laboratories may provide an enhanced safety profile for research studies on microorganisms in high and maximum containment laboratories.

- Finite Laboratory Lifespan. Biological laboratories have a finite lifespan and require replacement or refurbishment at the end of their useful life. In addition, given the long timelines involved in building laboratory capacity, planning for facility replacement must be done years before the facility can be closed or updated.

- Congressional Appropriations Processes. Several congressional appropriations bills fund U.S. Government agencies. Different appropriation bills are overseen by different congressional appropriations subcommittees. The congressional appropriations process does not have a mechanism to address the need for high-containment laboratories in totality across all departments and agencies.

Recommended Approach to Determine the Appropriate Number of High Containment U.S. Laboratories Required to Possess, Use, or Transfer BSAT

[56] K.F. Smith. Global rise in human infectious disease outbreaks. J. R. Soc. Interface 6 December 2014 vol. 11 no. 101 20140950

The need for medical countermeasures, diagnostic capabilities, and basic research on infectious agents and toxins highlights the national importance of and need for biocontainment facilities. Federal agencies must continually evaluate how to adapt their missions to protect human, animal and plant health against a constantly changing landscape of emerging diseases and novel opportunities as technology advances. These changes may require re-evaluation of biocontainment laboratory space needs within or across departments and agencies to remain current and viable. What follows is an approach recommended by the FESAP to determine the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT. In particular, it addresses the national amount of containment laboratory space that is subject, directly or indirectly, to U.S. Government oversight; it does not address containment space built and operated by nongovernment entities for nongovernmental missions. (As explained earlier, neither does it address containment space used for non-research missions such as clinical and diagnostic laboratories.) The FESAP recommends a methodology for periodic evaluation of laboratory space that focuses on alignment of mission with research needs, and on the phased incorporation of additional considerations and viewpoints such as enhancing both transparency and public trust in the federal process for decisions. This methodology utilizes a three-phase approach characterized by internal USG review, review by an external non-federal entity, and consideration of the external non-federal entity's review by the U.S. Government (See *Figure 1*.)

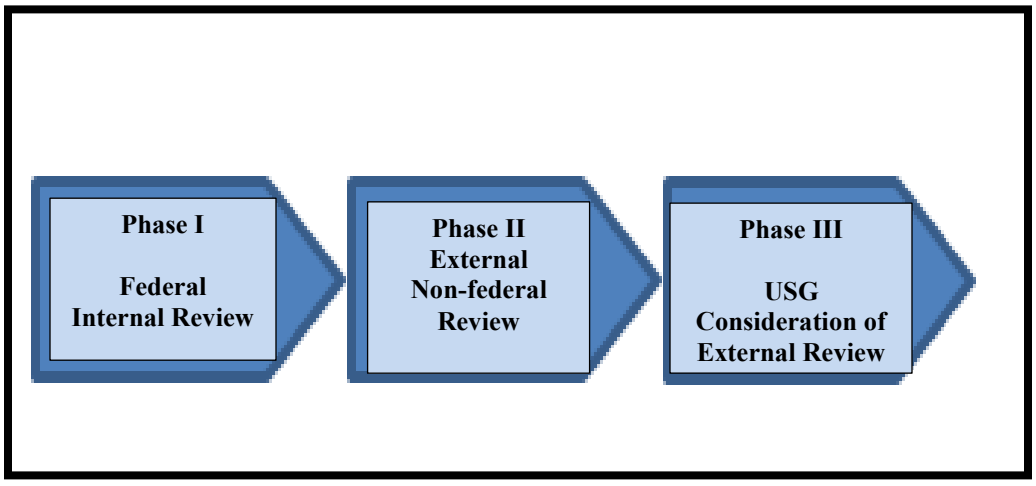

Figure 1. The recommended approach to determine the appropriate number of high containment U.S. laboratories required to possess, use, or transfer BSAT is a three phase process characterized by federal assessment, external non-federal review, and consideration of the recommendations of the external review by the U.S. Government.

Given the diversity of federal department and agency missions and the need for high containment laboratories to meet mission requirements, a successful process should begin with assessment of agency needs, mission, and capabilities prior to implementing a strategic evaluation across all departments and agencies. Therefore, Phase I consists of an internal federal review that involves the identification of best practices in determining and filling the need for such space, along with articulating the assumptions federal agencies make in determining their future containment space needs. This internal federal review will first address space built and/or operated by the Government. Once this review is completed, possible methodologies will be examined for assessing the need for space operated by non-governmental entities that is available for federally-funded research.

In the three phase approach, Phase II calls for an external review by a non-federal entity of the internal federal examination and is intended to validate or suggest modifications to the results of the federal examination, provide recommendations for any changes to process or additional factors to be considered, and ensure public confidence in the review process. This external review provides the opportunity to identify factors important to determining the appropriate amount of national containment laboratory space that federal agencies may not have sufficiently considered in their individual processes.

Finally, Phase III involves the consideration and implementation of external recommendations by the U.S. Government, as appropriate. The U.S. Government would adopt best practices where possible and ensure that adopted recommendations are in accordance with federal legal, regulatory, and department and agency requirements. Each phase would include examination of existing laboratory space capacity and its alignment with department and agency missions to identify opportunities to optimize the use of high containment laboratory space to help achieve national priorities.

The proposed approach intentionally does not focus on a review of specific projects or proposals, or retroactively modify the analysis and review procedures that pending projects have undergone. Instead, it comprises a strategic evaluation of Government's future procedures for meeting the nation's containment laboratory space requirements. If desired, such a comprehensive review process could be repeated at some time interval appropriate to the long time lines for laboratory construction. As scientific techniques advance, new diseases emerge, and national priorities shift over time, it may be necessary to conduct a periodic examination to determine the adequacy and distribution of high-containment laboratory space to address strategic national needs.

Identification of an Approach to Determine the Appropriate Number of High Containment U.S. Laboratories Required To Possess, Use, or Transfer BSAT

The recommended approach to determine the appropriate number of federally funded high containment U.S. laboratories required to possess, use, or transfer BSAT is a three phase process characterized by federal assessment (Phase I), external non-federal review (Phase II), and consideration of the recommendations of the external non-federal review by the U.S. Government (Phase III). The proposed three phase process will include development of a general USG 'best practices checklist' for departments and agencies to follow when they are considering the need to modify existing or add additional high and maximum containment laboratory space capacity.

Phase I: Federal Assessment

Phase I includes an internal federal review of the capacity needs for high containment space, and of the process that is used to address capacity needs. This review is comprised of two steps—1) the federal departments or agencies conduct an independent assessment of their need for high containment space based on mission requirements and in alignment with their strategic plans, and identify the steps they would use to address these needs, and 2) a review by a federal interagency panel of the need for high containment space based on national needs, and of the processes by which agencies meet those needs. The outcome will be a 'best practices checklist' that will be used as a guideline by departments and agencies when considering the construction of high or maximum containment laboratories. The best practices checklist will ensure that departments and agencies have considered the many different potential options to address their containment research needs and could potentially enable a reduction in the time and cost for planning; design; the release of the request for funding; the award; and the construction of high and maximum containment laboratories.

Step 1 of Phase I is addressed independently by federal departments or agencies. Step 2 of Phase I involves a federal interagency review panel. The federal interagency review panel should be carefully chosen to ensure the least possible conflict of interest for participants and the most objective expert review possible, while retaining the ability to draw on relevant technical experts in the respective departments and agencies. The federal interagency review panel can provide general direction and guidance to the D/A, but should not be involved in formal approval of specific D/A plans to add to or reduce high containment laboratory space.

Department and agency independent assessment of current and projected space needs

Step 1: **Individual departments and agencies will independently examine the use and availability of high containment laboratory space, including the process they use to**

acquire the necessary containment laboratory space. Departments and agencies will address how they meet mission requirements in relationship to their strategic plans with the goal of preparing an overall assessment of available space to meet current and projected needs.

Individual departments and agencies will:

- Examine their mission in the context of high containment space to ensure it can meet mission requirements.
- Articulate information about methodology used to assess current and projected space use.
- Articulate assumptions made in projecting future space requirements.
- Provide information about the adequacy of current space and available space to meet current and projected needs.
- Identify any concerns related to use of available space.
- Identify gaps in the use of available space.
- Identify "best practices" for a checklist that could be generally used by other departments and agencies to streamline the process of planning and designing containment space.
- Provide an overall assessment of current and projected needs to meet their mission requirements.

Federal Review Panel Assessment

Step 2: **Federal interagency review panel will examine department and agency assessments in totality**

The federal interagency review panel will:

- Review the planning assumptions with respect to future laboratory space requirements and achieve consensus, where possible, on any assumptions that would relate to more than one department/agency's plans.
- Provide an overall assessment of department and agency assessments to meet current and projected national needs.
- Identify overall projected high containment space needs and/or opportunities for more effective use of existing space and optimization of efficiencies, where possible.
- Provide strategic advice related to alignment of current and projected department and agency high containment laboratory capacity needs with national needs.
- Develop generalizable principles, standardized methodologies, and templates (e.g., "best practices" checklist) that could be applied to guide assessments of current and projected needs for high containment space, as well as mechanisms to efficiently meet those needs.
- Develop criteria and design a mechanism for external stakeholder review and analysis.

Phase II: External Review Panel Assessment

***Step 3*: Establish an external non-federal entity to examine the outcome of Phase I in the context of national needs.**

The Phase II review, conducted under criteria developed in Phase I, provides the opportunity for review of USG plans from a perspective broader than that of any single agency. This review can consider factors such as aggregate national need and can provide perspective on potential efficiencies resulting from collaborative work that agencies might not have identified. It also provides the opportunity to consider factors relating to the optimal amount of national biocontainment space that individual agency assessments may not have considered. The step provides a mechanism for an objective assessment of laboratory use and needs and would help to enable further transparency and public trust and confidence related to the number of high containment laboratories.

The external non-federal entity will:

- Validate (or make suggestions for revision of) overall needs and gaps in high containment space in meeting current capacity needs.
- Validate (or make suggestions for revision of) overall projected high containment space needs.
- Provide an overall assessment of the federal review panel's overall assessment to meet current and projected national needs.
- Provide strategic advice related to current and projected high containment needs to meet national needs.
- Identify factors relating to the optimal amount of national biocontainment space that individual agency assessments may not have considered or that may fall outside the purview of the Executive Branch.
- Identify potential efficiencies that could result from collaborative work that agencies may not have identified.
- Validate (or make suggestions for revision of) generalizable principles that can be applied to guide assessments of the current and projected need for high containment space, as well as mechanisms to efficiently meet those needs.

Phase III: USG Consideration of External Review Panel Assessment

***Step 4*: The USG will carefully consider the assessment resulting from Phase II to ensure any recommendations are practical, implementable and appropriately incorporated into agency planning processes.**

Recommendations resulting from Phase II of this process will be examined by an internal federal government group to ensure high containment space considerations have been addressed by federal department and agency processes. Recommendations may include actions external to a single federal department or agency.

The USG will:

- Consider the assessment developed by the non-federal entity to ensure any recommendations are practical and can be implemented.
- Encourage implementation of recommendations in a consistent approach by various federal departments and agencies.
- Consider the development of a central clearinghouse or a mechanism to collect best practices for considerations related to proceeding to design and build once decision is made.
- Provide general direction and guidance to departments and agencies considering modifying high containment laboratory capacity - without assuming a formal approval of specific department and agency high containment laboratory space decisions.
- Develop a standardized mechanism, at the whole-of-government level, to formally acknowledge the accession of new space.

Report of the Federal Experts Security Advisory Panel

Glossary[57]

Accreditation – For the purposes of this report, the term accreditation refers to an objective assessment of an institution's biosafety/biocontainment or biorisk management program by an independent body. Accreditation would allow the institution to demonstrate that its biosafety and biocontainment programs meet or exceed national standards. This approach is comparable to the CEN laboratory biorisk management standard,[58] which indicates "… a biohazard, or biorisk management program is that part of an organization's management system used to develop and implement its policy established to manage its biohazards. A management system approach to biohazard risks implies that identifying, understanding and managing a system of interrelated processes for a given objective, improves the organization's effectiveness and efficiency."

All sectors – The term "all sectors," as used in the Task Force report, refers to government (federal, State, Tribal, and municipal), academia, privately funded research institutions, and private industry.

Animal biosafety levels (ABSL) – Designations of laboratories in ascending order based on the degree of risk associated with the work being conducted. The designations ABSL-1, ABSL-2, ABSL-3, ABSL-3 "enhanced,"[59] and ABSL-4[60] are for work with biohazards used in a vivarium that include zoonotic or human pathogens.

Applied biosafety and biocontainment research – Research designed to generate science-based practices and procedures, engineering controls, personal protective equipment, and risk-assessment methodologies necessary to optimize the safety of research facilities; and to keep safety equipment, practices, and procedures up to date.

Biocontainment – A term used differently in facilities for the study of human pathogens versus those used for the study of agricultural pathogens. *1. In agricultural facilities*, the definition for "biocontainment" resembles that for "biosafety," i.e., the safety practices

---

[57] Definitions in glossary were excerpted from the *Report of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.* See http://www.phe.gov/preparedness/legal/boards/biosafetytaskforce/Pages/default.aspx. (pages 129-139)

[58] CEN is the European Committee for Standardization (Comité Européen de Normalisation). The September 2011 version of the CEN document, entitled *Laboratory Biorisk Management* (CWA 15793) is available at http://www.internationalbiosafety.org/ResourceManager.aspx?MenuItemID=3171d3a4-2ae5-40a0-bee6-ed41c3c8db19 , under Guidelines and Standards, Biorisk Management. .

[59] For some animal select agents, USDA/APHIS identifies "BSL-3 enhanced" laboratories for *in vitro* activities, and "ABSL-3 enhanced" for *in vivo* activities.

[60] The acronyms ABSL-1 through ABSL-4 are defined in the *BMBL* as "Vertebrate Animal Biosafety Levels" (see Chapter II, Table 2) and relate to combinations of engineering controls, safe practices, and safety equipment used to contain biological hazards in animal facilities.

and procedures used to prevent unintended infection of plants or animals or the release of high-consequence pathogenic agents into the environment (air, soil, or water). *2. However, for all high and maximum containment facilities*, "biocontainment" also refers to the physical containment barriers in a facility such as contained dressing and shower rooms, sealed service penetrations, specialized doors, entry and exit avenues to prevent cross-contamination, specialized air handling systems for contamination control, personal protective equipment, biosafety cabinets, etc.

Biohazard – A contraction of the words "biological" and "hazard." A biohazard is an infectious agent or hazardous biological agent or part thereof regardless of origin (naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance) that presents a real or potential risk to humans, animals, or plants, either directly through infection, or indirectly through the disruption of the environment. Biohazards include certain types of recombinant DNA; organisms and viruses that cause infections in humans, animals, or plants (e.g., parasites, viruses, bacteria, fungi, prions, rickettsia); and other biologically active agents (e.g., toxins, allergens, venoms) that may cause disease in living organisms, or adversely affect the environment, community, commerce, or trade agreements.

Biological agent – Any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment. (From the CDC Select Agents and Toxins Final Rule. 72 CFR 73.1 Definitions).[61]

Biorisk – Combination of the probability of occurrence of harm and the severity of that harm where the source of harm is a biological agent or toxin (adapted from ISO/IEC Guide 51:1999).

Biosafety – The application of combinations of laboratory practices and procedures, laboratory facilities, safety equipment, and appropriate occupational health programs when working with potentially infectious microorganisms and other biohazards.[62] Biosafety practices and procedures are designed to reduce the exposure of laboratory personnel, the public, agriculture, and the environment to potentially infectious agents and other biological hazards. The key principles of biosafety are risk assessment and containment. The principles of biosafety have been articulated in two key reference documents, the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic*

[61] The *SAR* are available at http://www.selectagents.gov/regulations.html

[62] Definition adapted from the BMBL 5th Ed. See: http://www.cdc.gov/biosafety/publications/bmbl5/index.htm.

Acid Molecules[63](first published in 1976), and BMBL[64] *(*initially issued in 1984). These documents have both been amended and revised over the years to reflect advances in science and technology. For more than two decades, the *BMBL* has been the code of practice for biosafety in the United States.

Biosafety and biocontainment oversight – The multi-tiered, often-overlapping system—from principal investigators at individual laboratories to agencies of the Federal Government—that seeks to ensure the safety of biological laboratories and their activities through compliance with existing laws, regulations, policies, standards, and guidelines on biosafety and biocontainment. The deliberate redundancy in the biosafety and biocontainment oversight framework helps ensure the protection of laboratory workers, animals and plants, the food supply, the public, and the environment from exposure to hazardous agents and toxins used in laboratories.

Biosafety level (BSL) – A designation of a laboratory in ascending order based on the risk associated with the work being conducted. The designations BSL-1, BSL-2, BSL-3, and BSL-4 are for work with human pathogens and are based on the utilization of combinations of engineering controls, safe working practices, laboratory facility design, and safety equipment. Each combination is specifically appropriate for the laboratory operations performed, the documented or suspected routes of transmission of the infectious agents utilized or stored in the laboratory, and the laboratory function or activity. The assignment of a biosafety level to a particular work process or research protocol is made through protocol-driven risk assessment, so that potential hazards specific to the work can be identified and mitigated effectively. The "BSL" term for laboratory designation does not apply to plant pathogens. However, plant pathogens are typically contained in laboratories and greenhouse facilities equivalent to BSL-1, BSL-2, and BSL-3 laboratories.

Biosafety level-3-Agriculture (BSL-3-Ag) – A unique containment level defined by USDA for work with large agricultural species that cannot be housed in primary containment devices. These species require that facility barriers usually used as secondary barriers now serve as the primary barrier.

Biosafety officer (biological safety officer or BSO) – An individual who acts as a technical resource to scientific and management staff by assisting in the conduct of risk assessments and risk management involving work with biological hazards including recombinant DNA. BSOs promote compliance with biosafety and biocontainment regulations, guidelines, and policies in each laboratory, and assist in the development of emergency response plans. This position and its suggested function(s) are described in

[63] The *NIH Guidelines* are available at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.
[64] For the online fifth edition of the *BMBL*, see http://www.cdc.gov/biosafety/publications/bmbl5/index.htm. .

several documents such as the *NIH Guidelines*, WHO *Laboratory Biosafety Manual*, Third Edition, and the Army Pamphlet (DA PAM) 385-69.[65]

Biosafety professional – The term used in this report to indicate a professional highly trained in biosafety and biocontainment principles and practices (e.g., a BSO or equivalent) who promotes safe laboratory practices, procedures, and proper use of containment equipment and facilities; stimulates responsible activities among workers; and provides advice on laboratory design. Regardless of their initial training (e.g., as microbiologists, biologists, molecular biologists, environmental health professionals, industrial hygienists, clinical health care professionals, veterinarians, and engineers), biosafety professionals must develop knowledge of the principles of epidemiology, disease transmission patterns, risk-assessment/ risk management methodology, disinfection and sterilization techniques, disease prevention, aerobiology, and environmental control. Biosafety professionals work in concert with other laboratory personnel who handle pathogenic or potentially infectious microorganisms, recombinant DNA molecules and organisms containing them, and biological toxins.[66] They typically serve on biosafety review committees, and are involved in the development and implementation of institutional biosafety/biocontainment management programs. Ideally, biosafety professionals, BSOs, and their equivalents should be credentialed (registered or certified) by a responsible entity.

Biosafety review committee –The term used in this report to refer to a group of individuals affiliated with a facility whose functions typically extend beyond those of the "institutional biosafety committee" (IBC) as described in the *NIH Guidelines*. Suggested functions for a biosafety review committee also are described in other documents including the WHO *Laboratory Biosafety Manual*, Third Edition, and the Army biosafety pamphlet DA PAM 385-69. Common roles of a biosafety committee include participation in development of institutional biosafety policies and codes of practice and risk assessments based on reviews of laboratory protocols for work involving hazardous biological agents, recombinant DNA other genetically modified materials, and potentially hazardous synthetic agents. Other functions of the committee may include the formulation of new safety policies and arbitration in disputes over safety matters.[67]

Biosecurity – The term denotes the protection of hazardous biological agents, including toxins, from loss, theft, diversion, or intentional misuse.

---

[65] *The NIH Guidelines* (Section IV-B-3) are available at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines; the Army, DA PAM 385-69 (section 3-3) is available at www.apd.army.mil/pdffiles/p385_69.pdf.; and the WHO *Laboratory Biosafety Manual*, Third Edition, is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf.

[66] Information adapted from the ABSA description of the biological safety profession, available at http://www.absa.org/biosafety.html.

[67] ibid Footnote 65.

Certification – A term used differently in different contexts to refer to the process of validating the expertise and credentials of an individual or an engineering control and in some cases a laboratory facility. *1. For an individual*, "certification" refers to a valuable step in professional development. Individuals pursuing certification must demonstrate they meet established educational criteria, and must also meet the prerequisite experience relevant to the area in which certification is being sought. Relevant experience is experience in which a significant majority of the candidate's duties is in the area in which he/she is seeking certification. After the certifying body has verified, through a review of relevant documents, that the individual has met both requirements, the individual will be eligible to sit for a certification exam, which will test their knowledge in the area they are seeking certification. *2. For an engineering control* which, in many cases will have two distinct types of certification; i.e., biological safety cabinets (BSC) have design certification to a standard and a field operation standard. BSC design certification is formal validation by a qualified design testing organization that a designated cabinet model meets all the requirements of National Sanitation Foundation (NSF) Standard 49, annex A; whereas BSC Field Certification is formal verification by a qualified field testing certifier that an installed cabinet meets all the requirements of NSF Standard 49, annex F of this standard. *3. For a facility*, the term "certification" is not widely used, and is not based upon an internationally recognized standard (e.g., as is the case for BSC design, per NSF 49). For the purposes of this report, facility certification refers only to the National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements, which describes the systematic review of all safety features and processes associated with the laboratory (engineering controls, personal protective equipment, building and system integrity, standard operating procedures [SOPs] and administrative controls, such as documentation and record retention systems).[68] This validation assures that all reasonable facility controls and prudent practices are in place to minimize, to the greatest extent possible, the risks associated with laboratory operations and the use of biohazardous materials.

Clinical laboratory − A workplace where diagnostic or other screening procedures are performed on blood or other potentially infectious materials.

Entity − Any government department or agency (federal, state, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity. (From the CDC *Select Agents and Toxins Final Rule*. 72 CFR 73.1 Definitions)

Federal agency – *1.* An agency of the Executive branch of the Federal Government as defined in section 105 of title 5, United States Code. *2.* With respect to any research facility, the agency from which the research facility receives a federal award for the conduct of research, experimentation, or testing.

[68] Definition adapted from the "National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements," available at http://www.ors.od.nih.gov/sr/dohs/Documents/bsl3_certguide.pdf.. NIH uses the term "certification" to refer to a laboratory, whereas other entities typically refer to "accreditation" of a facility.

Federal funding – Money awarded via a mechanism (grant, award, loan, contract, or cooperative agreement) under which federal funds are used to support the conduct of research, experimentation, testing, or infrastructure (expansion, construction, or maintenance of a facility).

Guidelines – Standards or principles written by an organization to assist in the effectiveness of an operation, or to recommend a course of action. The *BMBL*, for example, describes guidelines for laboratory biosafety and biocontainment. Unlike regulations, guidelines do not carry the force of law.

High and maximum containment − The term used in this report to describe BSL-3 and BSL-4 laboratories and equivalent containment facilities, i.e., animal facility/vivarium ABSL-3 and ABSL-4, and biosafety level-3 agriculture (BSL-3Ag) facilities. More specifically, "high containment" refers to BSL-3 and equivalent containment facilities, whereas "maximum containment" refers to BSL-4 and equivalent containment facilities. The research activities that occur in high and maximum containment facilities include studies of hazardous pathogens that infect humans, zoonotic agents, toxins, and a range of agricultural pathogens, which include foreign and emerging agricultural agents that can infect livestock and crops. For the purposes of this report, the terms "BSL-3, BSL-4, and equivalent agricultural containment facilities" and "high and maximum containment facilities" are synonymous.

Incident − For the purposes of this report, a laboratory event that may include exposure of staff or the public to an infectious, potentially infectious, or zoonotic agent; environmental release of a biological hazard; escape of infected animals or vectors; spill of a biohazard outside of a primary containment device; loss or theft of biohazardous agents and other loss of containment; or equipment failure in conjunction with a biohazard (e.g., centrifuge accident) that may lead to a release of a hazardous agent within the laboratory environment or outside the laboratory environment. An incident or accident can cause a laboratory-acquired illness (LAI).[69]

Infectious substance − A material known to contain or reasonably expected to contain a pathogen.

Institutional biosafety committee (IBC) – A committee comprised of no fewer than five members so selected that they collectively have experience and expertise in recombinant DNA technology and the capability to assess the safety of recombinant DNA research and to identify any potential risk to public health or the environment.[70]

Laboratory-acquired infection (LAI) – An infection resulting from exposure to an infectious agent in a laboratory.

[69] Definition of incident/accident was drafted by USDA/ARS to describe the agency's biohazard incident reporting procedure, which includes reporting of laboratory-acquired illnesses.
[70] From the *NIH Guidelines*, Section IV-B-2-a-(1).

Microbe – A microscopic organism, such as a bacterium, fungus, protozoan, or virus.

Pathogen − A microorganism (including bacteria, viruses, rickettsiae, parasites, fungi) or other agent, such as a proteinaceous infectious particle (prion) that can cause disease in humans, animals, or plants.

Personal protective equipment (PPE) – Specialized clothing or equipment worn by an employee for protection against a hazard. General work clothes (e.g., uniforms, pants, shirts or blouses) not intended to function as protection against a hazard are not considered to be personal protective equipment.

Personnel reliability – In the context of life sciences research, an assurance that individuals with access to dangerous pathogens are trustworthy, reliable, and physically and mentally competent.

Production facility – A facility engaged in industrial-scale, large-volume or high concentration of microbes.

Policy – A principle, plan, or course of action. The term may apply to the Federal Government, State and local (municipal) governments, private sector organizations, groups, and individuals. The Executive branch of the Federal Government can establish policy through the use of both regulations and guidance documents.

Principal investigator (PI) – The individual designated by a research entity to direct a project or program, and who is responsible to the entity for the scientific and technical direction of that project or program. (Adapted from the CDC *Select Agents and Toxins Final Rule*, 72 CFR 73.1, Definitions)

Recombinant DNA (rDNA) – (i) Molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i). (From the *NIH Guidelines* Section I-B)

Regulation – A rule based on a statute. *1.* For the purposes of this report, a federal regulation is a statement by a federal agency[71] designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency promulgated in accordance with the *Administrative Procedure Act*. Once adopted, a federal regulation is legally binding. The *SAR* are an example of biosafety and biosecurity regulations. *2.* State and local regulations are administrative rules or directives developed by State and local officials in addition to federal regulations. Once adopted, a state or local regulation is legally binding.

[71] Federal agency and agency are defined in 5 U.S.C. 101 and 105.

Research – As used in this report, a systematic investigation aimed at the discovery or interpretation of facts, revisions of accepted theories or laws in the light of new facts, or practical application of such new or revised theories or laws, including the processes of experimentation, development, testing, and evaluation.

Risk assessment – A process used to identify the hazardous characteristics of a known infectious agent or potentially infectious agent or material, the activities that can result in exposure to such an agent, the likelihood that such exposure will cause a laboratory-acquired infection (LAI), and the probable consequences of such an infection. The key principle in selecting the appropriate safeguards for the conduct of the microbiological research or work at hand is "risk assessment." The information identified through risk assessment is used to guide the selection of appropriate microbiological practices, safety equipment, and facility safeguards that, when used properly, can prevent exposures and dramatically reduce the incidence of LAIs. Risk assessment is a common first step in an overall risk-management process. This approach has been used successfully for decades to allow the safe conduct of microbiological research and manipulation of clinical microbiological specimens. (Adapted from the *BMBL*)

Select agents and toxins – Federally regulated biological agents (e.g., viruses, bacteria, fungi, and prions) and toxins that have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products. The latter agents are also referred to as high-consequence livestock pathogens and toxins, non-overlap agents and toxins, and listed plant pathogens. Select agents and toxins are defined by lists (see below) that appear in sections 73.3 of Title 42 of the Code of Federal Regulations (HHS/CDC *SAR*), sections 121.3 and 121.4 of Title 9 of the Code of Federal Regulations (USDA/APHIS/Veterinary Services (VS) *SAR*), and section 331.3 of Title 7 of the Code of Federal Regulations (plants - USDA/APHIS/PPQ *SAR*) and Part 121, Title 9, Code of Federal Regulations (animals – USDA/APHIS). Select agent and toxins that are regulated by both HHS/CDC and USDA/APHIS are referred to as "overlap" select agents and toxins (see 42 CFR 73.4 and 9 CFR 121.4). (For the current lists of select agents and toxins, see http://www.selectagents.gov/SelectAgentsandToxinsList.html.

Select Agent Program – A federal program run by the U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) that is designed to monitor and regulate the possession, use, or transfer of select agents or toxins that could pose a severe threat to public health and safety; to animal or plant health; or animal or plant products. The *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* and the *Agricultural Bioterrorism Protection Act of 2002* (the Acts) require entities to register with the HHS Centers for Disease Control and Prevention (CDC) or the USDA Animal and Plant Health Inspection Service (APHIS) if they possess, use, or transfer select agents or toxins. In addition to ensuring that laboratories handle these select agents and toxins safely, the Acts also require increased safeguards and security measures for these agents, including controlling access, screening entities and personnel (i.e., security risk assessments), and establishing a comprehensive and detailed national database of registered entities. The Acts also impose criminal and civil penalties for the inappropriate use of select agents and toxins.

Toxin – The toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever their origin and method of production, and includes any poisonous substance or biological product that may be engineered as a result of biotechnology, produced by a living organism; or any poisonous isomer or biological product, homolog, or derivative of such a substance. (From the CDC *Select Agents and Toxins Final Rule*, 72 CFR 73.1, Definitions)

ABBREVIATIONS AND ACRONYMS

ABSA	American Biological Safety Association
ABSL	Animal biosafety level
A/E	Architecture and Engineering
AHRQ	Agency for Healthcare Research and Quality
AIDS	Acquired Immune Deficiency Syndrome
ANSI	American National Standards Institute
APHIS	Animal and Plant Health Inspection Service (USDA)
ASHRAE	American Society of Heating, Refrigerating and Air Conditioning Engineers
ARS	Agricultural Research Service (USDA)
ASM	American Society of Microbiology
ASSE	American Society for Safety Engineers
BARDA	Biomedical Advanced Research and Development Authority (HHS)
BMBL	*Biosafety in Microbiological and Biomedical Laboratories*
BSAT	Biological Select Agents and Toxins
BSL	Biosafety level
BSO	Biological Safety Officer
BSC	Biological safety cabinet
CBDP	Chemical and Biological Defense Program
CBR	Chemical, biological, or radiological
CBRN	Chemical, biological, radiological, and nuclear
CBSP	Certified Biological Safety Professional
CDC	Centers for Disease Control and Prevention
CEN	European Committee for Standardization (French: Comité Européen de Normalisation)
CFR	Code of Federal Regulations
COE	Center of Excellence
CVB	Center for Veterinary Biologics
DHS	Department of Homeland Security
DNA	Deoxyribonucleic acid
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOJ	Department of Justice
DOL	Department of Labor
DOS	Department of State
DOT	Department of Transportation

EH&S	Environmental Health and Safety
EIS	Environmental Impact Statement
EPA	Environmental Protection Agency
FAA	Federal Aviation Administration
FAD	Foreign Animal Disease
FADRU	Foreign Animal Disease Research Unit
FADT	Foreign Animal Disease Threats
FBI	Federal Bureau of Investigation
FDA	Food and Drug Administration
FDWSRU	Foreign Diseases and Weed Science Research Unit
FESAP	Federal Experts Security Advisory Panel
FSAP	Federal Select Agent Program
FSIS	Food Safety and Inspection Service (USDA)
HEPA	High-efficiency particulate air
HHS	(Department of) Health and Human Services
HIV	Human Immunodeficiency Virus
HPAI	Highly pathogenic avian influenza
HSPD	Homeland Security Presidential Directive
IAA	Interagency Agreement
IBC	Institutional Biosafety Committee
IRF	Integrated Research Facility
LAI	Laboratory-acquired infection
LPAI	Low pathogenic avian influenza
LRN	Laboratory Response Network
MCM	Medical countermeasures
MD	Management Directive
NAHLN	National Animal Health Laboratory Network
NAS	National Academies of Sciences
NASA	National Aeronautics and Space Administration
NBACC	National Biodefense Analysis and Countermeasures Center
NBAF	National Bio- and Agro-Defense Facility
NBBTP	National Biosafety and Biocontainment Training Program
NEIDL	National Emerging Infectious Diseases Laboratory
NIAID	National Institute of Allergy and Infectious Diseases
NICBR	National Interagency Confederation for Biological Research
NIH	National Institutes of Health
NIH Guidelines	*NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*
NPDN	National Plant Diagnostic Network
NPI	National Pathogen Inventory

NRCM	National Registry of Certified Microbiologists
NSC	National Security Council
NSF	National Science Foundation
NVSL	National Veterinary Services Laboratories
OBA	Office of Biotechnology Activities
ODNI	Office of the Director of National Intelligence
OIE	World Organization for Animal Health (French: e Office International des Epizooties)
OIG	Office of the Inspector General
OMB	Office of Management and Budget
OSHA	Occupational Safety and Health Administration
OSTP	Office of Science and Technology Policy
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PHS	Public Health Service (HHS)
PI	Principal Investigator
PIADC	Plum Island Animal Disease Center
PPE	Personal Protective Equipment
PPQ	Plant Protection and Quarantine
R&D	Research and Development
RBSP	Registered Biological Safety Professional
RDT&E	Research, development, testing, and evaluation
RFI	Request for Information
RO	Responsible Official
SARS	Severe acute respiratory syndrome
SAIC	Science Applications International Corporation
SAR	Select agent regulations
SEPRL	Southeast Poultry Research Laboratory
SME	Subject Matter Expert
SOP	Standard Operating Procedure
SRA	Security Risk Assessment
SSRA	Site-Specific Threat and Risk Assessment
S&T	Science and technology
TB	Tuberculosis
T&E	Test and evaluation
U.S.	United States
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
U.S.C.	United States Code
USDA	United States Department of Agriculture
USG	U.S. Government

VA	Department of Veterans' Affairs
VS	Veterinary services

Report of the Federal Experts Security Advisory Panel

APPENDICES

APPENDIX A

Previous Recommendations of the Federal Experts Security Advisory Panel

The FESAP successfully completed the tasks enumerated by Executive Order 13546, "Optimizing the Security of Biological Select Agents and Toxins." The FESAP issued a report in November 2010 with recommendations on the following issues:

- the designation of Tier 1 BSAT;
- reduction in the number of BSAT on the Select Agent List;
- the establishment of appropriate practices to ensure reliability of personnel with access to Tier 1 BSAT at registered facilities;
- the establishment of appropriate practices for physical and cyber security for facilities that possess Tier 1 BSAT; and
- other emerging policy issues relevant to the security of BSAT.

Highlights of the FESAP's recommendations follow:

- **Designation of Tier 1 BSAT.**
  - The FESAP identified 20 criteria for use in determining appropriate Tier 1 BSAT, including the ability to produce a mass casualty event or devastating effects to the economy, communicability, low infectious dose, and a history of or current interest in weaponization based on threat reporting.
  - The FESAP proposed the designation of the following 10 select agents as Tier 1 BSAT: *Bacillus anthracis*, *Burkholderia mallei*, *Burkholderia pseudomallei*, Ebola virus, foot-and-mouth disease virus, *Francisella tularensis*, Marburg virus, Variola major virus, Variola minor virus, and *Yersinia pestis*.
  - At this time, the FESAP does not recommend including botulinum toxin and/or toxin-producing strains of *Clostridium botulinum* on the list of Tier 1 BSAT, and recommended that HHS and USDA use the rule-making process to solicit public comment regarding their inclusion.

- **Reduction in number of agents on the Select Agent List.**
  - The FESAP recommended the removal of 25 agents on the list including 7 HHS and HHS/USDA overlap agents, 12 USDA animal agents, and 6 toxins. The HHS and HHS/USDA overlap agents recommended for removal include: cercophithecine herpesvirus 1 (Herpes B virus),

Coccidioides posadasii, *Coccidioides immitis*, Eastern equine encephalitis virus (only South American genotypes), flexal virus, tick-borne encephalitis viruses (only European subtypes), and Venezuelan equine encephalitis virus (only enzootic subtypes ID and IE).

- Toxins recommended for removal from the select agent list include: *Clostridium perfringens* epsilon toxin, conotoxin, diacetoxyscirpenol, shiga toxin, shiga-like ribosome inactivating proteins, and T-2 toxin.

- **Establishment of appropriate practices to ensure the suitability and reliability of personnel who seek or have access to BSAT.**
  - The FESAP developed several recommendations which focus on enhancement of the current Security Risk Assessment (SRA) performed by the FBI, pre-access suitability assessment at the federal and local levels, and continued monitoring of personnel reliability at the local level.
  - The FESAP recommended that the current SRA process be enhanced and clarified to better assess disqualifiers and assess foreign nationals.
  - The SAP should provide guidance on pre-access suitability assessments of personnel to assist local entities in identifying the qualities of suitability for personnel who seek access to BSAT. Because elements of suitability can change over time (such as credit and criminal status), these should be periodically rechecked as part of an ongoing review of personnel reliability.
  - Finally, the SAP should provide guidance to entities regarding self- and peer- reporting of circumstances, conditions, activities, actions, or behaviors that may pose a safety or security concern.

- **Establishment of appropriate practices for physical security and cyber security for facilities that possess BSAT.**
  - Physical and cyber security encompass the application of operational and security equipment; personnel and procedures used to protect facilities; and information, documents or material for preventing or responding to theft, sabotage, diversion, or other terrorist or criminal acts.
  - For all facilities housing BSAT, the FESAP recommended the use of a Government-furnished risk assessment tool to ensure that facilities are consistently evaluating their vulnerability to particular threats, are implementing security measures appropriate to their level of risk, and to enable consistent inspection activities across multiple regulatory and oversight agencies.
  - Specifically for facilities that house Tier 1 BSAT, the FESAP recommended specific, enhanced performance standards to ensure the

physical and cyber security of the entity and BSAT. This enhanced security should be coordinated among all personnel responsible for aspects of security at a facility.

APPENDIX B

Membership of the Federal Experts Security Advisory Panel

Chairpersons:

Jere L. Dick, DVM
Associate Administrator
Office of the Administrator
Animal and Plant Health Inspection Service
Department of Agriculture
Washington, DC

George W. Korch Jr., PhD
Senior Science Advisor
Assistant Secretary for Preparedness and Response
Department of Health and Human Services
Washington, DC

Working Group Chairpersons:

Working Group 1: Identify needs and gaps and making recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT.

Carol D. Linden, PhD
Principal Deputy Director
Biomedical Advanced Research and Development Authority (BARDA)
Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services
Washington, DC

James B. Petro, PhD
Defense Threat Reduction Agency
Department of Defense

Working Group 2: Identify actions and any regulatory changes to improve biosafety and biosecurity.

Jason D. Bannan, PhD
Senior Scientist

Federal Bureau of Investigation
Department of Justice
Washington, DC

Robbin S. Weyant, PhD, RBP(ABSA)
Captain, USPHS (Ret.)
Director, Division of Select Agents and Toxins
Office of Public Health Preparedness and Response
Centers for Disease Control and Prevention
Atlanta, GA

Working Group 3; Identify an approach to determine the appropriate number of high-containment U.S. laboratories required to possess, use, or transfer BSAT.

Gerald L. Epstein, PhD
Deputy Assistant Secretary for Chemical, Biological, Radiological, and Nuclear Policy
U.S. Department of Homeland Security
Washington, DC

Steven Kappes, PhD
Deputy Administrator, Animal Production and Protection
Agricultural Research Service, National Programs
U.S. Department of Agriculture
Beltsville, MD

Membership of the FESAP and its three working groups included representatives from:

Department of Agriculture
Department of Commerce
Department of Defense
Department of Energy
Department of Health and Human Services
Department of Homeland Security
Department of Justice
Department of Labor
Department of State
Department of Transportation
Department of Veterans' Affairs
Environmental Protection Agency

National Science Foundation
National Security Council
Office of the Director of National Intelligence
Office of Science and Technology Policy
The Joint Chiefs of Staff

APPENDIX C

IDENTIFICATION OF GAPS/NEEDS, AND RECOMMENDATIONS TO OPTIMIZE BIOSAFETY, BIOSECURITY, OVERSIGHT, AND INVENTORY MANAGEMENT AND CONTROL

	Existing Regulations/ Guidance* (*listing is not comprehensive*)	Needs	Gaps	Recommendations
Biorisk Management (Biosafety and Biosecurity)	*CEN Workshop Agreement 15793 Laboratory Biorisk Management* *CDC/NIH Biosafety in Microbiological and Biomedical Laboratories* *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*	Mechanisms are needed by which individuals and the institutions in which they work are encouraged to implement and adhere to biosafety/biocontainment regulations, guidelines, standards, and policies in ways that further enhance safety and reduce risk. Achieving this objective will require strong support for local biosafety and biocontainment management programs from all levels of management at individual institutions where the research is conducted. It also may be necessary to improve existing mechanisms designed to ensure compliance.		**1.1 Culture of biosafety, biosecurity, and responsible conduct in the life sciences.** Create and strengthen a culture that emphasizes biosafety, laboratory biosecurity, and responsible conduct in the life sciences. This culture of responsibility should be characterized by individual and institutional compliance with biosafety and laboratory biosecurity regulations, guidelines, standards, policies and procedures, and enhanced by effective training in biorisk management.
Oversight	Occupational Safety and Health Act - General Duty Clause		Inconsistently applied policies at the local institutional level	**1.2 Appropriate Organizational and Governance Structure to Ensure Compliance**

	OSHA Standards, including: • Bloodborne Pathogens • Personal Protective Equipment Hazardous Waste Operations and Emergency Response Select Agent Regulations Laboratory Practice for Nonclinical Laboratory Studies Transportation of Etiologic Agents Export Administration Regulations		on use of an institutional biosafety committee or equivalent body to evaluate research protocols involving non-recombinant biological organisms.	**with Biosafety and Biocontainment Regulations and Guidelines.** Require that all research institutions in which human, plant, and/or animal infectious agents and toxins research is conducted have an appropriate organizational and governance structure to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines.
			Use of an institutional biosafety committee or equivalent body to evaluate research protocols involving inactivation, sterilization, or decontamination of biohazardous materials	**1.3 Appropriately Constituted Review Entity**. Require that an appropriately constituted and qualified review entity[72] validate local policies, laboratory protocols, and mitigation plans involving the inactivation, sterilization, or decontamination of biohazardous materials at research institutions.

[72] An example of an appropriately constituted review entity is the institutional biosafety committee (IBC, as described in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* [*NIH Guidelines*]) or its equivalent. The role of the IBC has expanded at many institutions. *The NIH Guidelines* are available at: http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.

Biosecurity		Promote a culture of security awareness in the life sciences community	Support for formal training/education on security awareness, threats, and history of biosecurity	**1.4 *Security Awareness Education Programs/Curriculum Development.** Support the development and implementation of security awareness education programs/curriculum that: ▪ Underscore personal responsibility for safeguarding potentially hazardous biological agents; ▪ Share information about security breaches that have occurred involving infectious or toxic materials; ▪ Emphasize the need for self and peer reporting; ▪ Discuss material protection strategies; and ▪ Explain exploitation of life sciences research.
Biosafety	*CDC/NIH Biosafety in Microbiological and Biomedical Laboratories* *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*	Need exists to promote awareness among all individuals who work in, oversee, or manage research and to provide training to address the importance of compliance with safety practices to minimize the risk of laboratory acquired infections and to		**1.5 Biosafety Awareness.** Develop and implement strategies to ensure effective communication and awareness of biosafety and biocontainment.

		protect the laboratory worker, the public, and agriculture.		
Biosafety		Applied biosafety and biocontainment research programs are needed to further develop science-based practices and procedures, engineering controls, personal protective equipment, and risk-assessment methodologies necessary to optimize the safety of BSL-3, BSL-4, and equivalent agricultural containment research facilities; and to keep safety equipment, practices, and procedures up to date.	Support for an applied biosafety research program Stakeholder feedback on applied biosafety research priorities, either through a Request for Information (RFI) or stakeholder meetings Collection of literature on applied biosafety, or applied environmental microbiology.	**1.6 Applied Biosafety Research.** Develop and maintain a robust federally-supported program of applied biosafety research to create additional evidence-based practices and technologies and to update existing practices and operations.
	OSHA record-keeping regulations Select Agent Regulations *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*	Although the OSHA record-keeping regulations,[73] SAR developed by HHS and the U.S. Department of Agriculture (USDA),[74] and *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic*		**1.7 Incident Reporting System.** Establish a new voluntary, anonymous, non-punitive incident-reporting system for research laboratories that would ensure the protection of sensitive and private information,

[73] Most high and maximum containment research facilities are exempt from OSHA record-keeping regulations, because OSHA has classified them as having low overall recordable work-related injuries and illnesses, in comparison to the national average for all industries.
[74] The *SAR* (7 CFR 331, 9 CFR 121, and 42 CFR 73) require reporting of the "theft, loss, or release" of a select agent or toxin. For more information about the *SAR*, see http://www.selectagents.gov/.

		Acid Molecules (*NIH Guidelines*)[75] include requirements to report laboratory incidents, there is no centralized, integrated incident-reporting and analysis system for all U.S. high and maximum containment research facilities in all sectors.		as necessary.
Inventory Management & Control	CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories* (Section VI) Select Agent Regulations, Section 11 (Security) and 17 (Records) Federal Select Agent Program Security Guidance document and guidance addressing long-term storage of select agents and toxins	Increased awareness about existing guidance and regulations is needed.	Inconsistently applied policies at the local institutional level on listing non-recombinant, non-select agent biological organisms and toxins with the institutional biosafety program.	**1.8 Material Accountability Procedures.** Increase awareness about existing material accountability best practices, and support the establishment of material accountability procedures where none currently exist.

*FBI is willing and prepared to provide materials that have already been developed for its biosecurity outreach and engagement activities

- U.S. Biological Weapons and Anti-Terrorism Criminal Statutes
- Spectrum of risk/threats (dual use/misuse, domestic/international terrorism, espionage, insider threat, workplace violence)
- History of the Select Agent Program

[75] The *NIH Guidelines* states that IBCs should report "...any significant problems, violations of the NIH Guidelines, or any significant research-related accidents and illnesses" to NIH OBA within 30 days. Appendix G of the *NIH Guidelines* specifies certain types of accidents that must be reported on a more expedited basis. For more information, see http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines.

APPENDIX D

Regulatory Framework for an Occupational Safety and Health Administration (OSHA) Infectious Diseases Standard

Background Information

OSHA is considering development of an Infectious Diseases standard to protect workers from exposure to infectious agents transmitted via the contact, droplet and airborne routes. OSHA has received comments on an Infectious Diseases Request for Information (RFI), and held stakeholder meetings (available at www.regulations.gov under docket OSHA-2010-0003). OSHA is currently considering feedback from small entity representatives regarding the economic and technological feasibility of this standard for small businesses that it could affect. The Infectious Diseases standard would cover healthcare and specific related settings such as laboratories. For laboratories, the Infectious Diseases standard would provide a mechanism to protect workers from infectious agent exposure by enforcement of the biosafety and biocontainment recommendations contained in guidance documents such as *BMBL*, *the NIH Guidelines* and clinical laboratory guidance documents such as CDC's *Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories. Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel* .[76]

Currently, laboratories are covered under OSHA standards such as the Bloodborne Pathogens (BBP) standard, the Respiratory Protection standard, and the Laboratory standard (which focuses on chemical hazards). Relevant OSHA standards and regulations include provisions for: PPE, illness and injury reporting, training, hazard evaluations, and hazard communication. In addition, the General Duty clause of the OSH Act (i.e., U.S.C. 654(a)(1)) requires that employers furnish every employee a workplace that is free from recognized hazards that cause or are likely to cause death or serious physical harm. Further, the whistleblower protection provision (i.e., U.S.C. 660(11)(c)) of the OSH Act prohibits employers from discriminating against their employees for exercising their rights under the OSH Act. Employers may also be responsible for complying with different or additional requirements in states that operate their own federally approved occupational safety and health programs.

Description of OSHA's Regulatory Framework for an Infectious Diseases Standard

[76] See http://www.cdc.gov/mmwr/preview/mmwrhtml/su6101a1.htm.

A) Scope (Would cover settings where workers have occupational exposure to infectious agents transmitted by the contact, droplet and airborne routes, during the provision of direct patient care and/or during the performance of other covered tasks).
   A) Key Elements of OSHA's Regulatory Framework for an Infectious Diseases Standard
      1) Worker Infection Control Plan (WICP) (Similar to a Biosafety Manual for Laboratories)
      2) Standard Operating Procedures (SOPs)
         i. **In all work settings, SOPS for:**
            a. Hazard evaluations
            b. Hand hygiene
            c. Restricted food and cosmetics
            d. Engineering, administrative and work practice controls including PPE; decontamination handling, containerization, transport and disposal of contaminated materials
            e. Occupational health services
            f. Emergency preparedness planning
            g. Exposure incident investigations
            h. Signage and labeling hazard communication during transport, shipping & receiving of infectious agents
         ii. **In settings where direct patient care is provided (e.g., hospitals, ambulatory care centers, long-term care facilities), SOPs for all work settings, and in addition, SOPs for:**
            a. Patient scheduling & intake/admittance
            b. Standard, contact, droplet and airborne precautions
            c. Patient transport
            d. Medical surge procedures
         iii. In settings where other covered tasks are performed (e.g., laundries, medical waste handling facilities, laboratories), SOPs for all work settings, and in addition, SOPs for:
            a. Handling and intake of contaminated materials
            b. Other necessary control measures to prevent or minimize transmission of infectious agents
            c. Engineering controls such as biosafety cabinets, lab hoods and other lab design and containment measures (specific for laboratories)
               i. Measures to address uncontrolled releases of infectious agents (specific for laboratories)
      3) Medical surveillance, vaccinations and medical removal protection for workers with occupational exposures
      4) Training

1. Limited recordkeeping requirements

How Flexibility Is Built In To the Regulatory Framework for an Infectious Diseases Standard

Given that facilities that would be affected by an Infectious Diseases rule have different potential sources of occupational exposure to infectious agents, and that facilities vary in terms of their capacity to address these sources of occupational exposure, OSHA's approach to an Infectious Diseases standard would be program-oriented (i.e., implementing a worker infection control plan) and largely performance-based. The OSHA regulatory framework does not reinvent the wheel, but instead is based on infection control regulations and guidelines that are already widely accepted (e.g., CDC guidelines).

The basic elements of infection control practice are laid out in CDC and NIH guidance documents. Not surprisingly, the guidance documents recommend similar basic practices (e.g., hand hygiene, decontamination of materials and surfaces, hazard signage and labeling) for different settings. However, the implementation of these infection control practices in different settings and under different conditions will be affected by a number of factors including:

- Characteristics of patient populations vary by setting. For example, large city hospitals see different types of patients than rural hospitals or physicians' offices.

- Types of infectious agents and diseases commonly encountered vary by setting. For example, active TB is more often seen in some states than in other states and more often seen in hospitals than in physicians' offices.

- Sources of worker exposure to infectious agents (e.g., patients, corpses, contaminated wastes and equipment, cultures of viruses or bacteria, etc.) vary by setting and by the types of tasks performed by workers. For example, workers in research and production laboratories are exposed to infectious materials while workers in healthcare settings and clinical laboratories are exposed to both infectious patients and materials.

- Frequency and duration of worker exposure to infectious agents varies by setting and by tasks performed. For example, workers in hospitals, nursing homes and laboratories are exposed to infectious patients and/or infectious materials on a daily basis while exposure may be less frequent in a physician's office.

- Characteristics (e.g., route of transmission) of the infectious agent(s) encountered will affect the nature and extent of worker exposures; the infectious agent(s) encountered vary by setting and by tasks performed.

The regulatory framework for OSHA's Infectious Diseases rule would not be "one size fits all," but instead would give covered employers considerable flexibility in tailoring their worker infection control plan to their specific settings and circumstances. OSHA's complete infectious diseases regulatory framework is available at www.regulations.gov under docket number OSHA-2010-0003.

APPENDIX E

Examples of Assessments of Research and Development Needs

Federal Experts Security Advisory Panel (FESAP) Examples of Assessments of Research and Development Needs			
Year	**Sponsor**	**Title and Link (if available)**	**Description**
Federal			
2013	EOP/NSTC	*Biological Response and Recovery Science and Technology Roadmap* http://www.whitehouse.gov/sites/default/files/microsites/ostp/NSTC/brrst_roadmap_2013.pdf	The report categorizes key scientific knowledge gaps, identifies technology solutions, and prioritizes research areas to enable government, at all levels, to make decisions more effectively during the response to and recovery from a biological incident—whether naturally occurring or intentional.
2013	EOP/NSTC	*National Biosurveillance Science and Technology Roadmap* http://www.whitehouse.gov/sites/default/files/microsites/ostp/biosurveillance_roadmap_2013.pdf	This document identifies and prioritizes Research and Development (R&D) needs with the goal of giving decision makers at all levels of government more accurate and timely information when biological incidents threaten health. Such incidents—whether the result of natural evolutionary causes, accidental releases or exposures, or malevolent activities—have the potential to erupt suddenly and evolve quickly. Surveillance can be key to predicting and even preventing such incidents, and can help minimize the impacts of incidents that cannot be prevented.
2013	Department of the Interior (DOI)	*USGS Ecosystems Science Strategy: Ecosystems Science Strategy—Advancing Discovery and Application through Collaboration* http://pubs.usgs.gov/circ/1383c/	This document describes a 10-year strategy to address priority environmental and resource management challenges for the U.S. Geological Survey (USGS) Ecosystems Mission Area. The strategy articulates a vision to improve understanding of how and why ecosystems change and explains how USGS ecosystem science can help inform managers and policy-makers to sustain and restore natural resources, protect vital ecosystem services, and secure the long-term health and economic well-being of U.S. citizens.
2013	DOI	*USGS Environmental*	This strategy describes how USGS will address

		Health Science Strategy—Providing Environmental Health Science for a Changing World http://pubs.usgs.gov/circ/1383e/	the highest priority environmental health issues facing the Nation. The ultimate intended outcome of this science strategy is prevention and reduction of adverse impacts to the quality of the environment, the health of our living resources, and human health.
2012	Department of Health and Human Services (HHS)/Food and Drug Administration (FDA)	*FDA Medical Countermeasures Initiative Strategic Plan. 2012-2016* http://www.fda.gov/downloads/EmergencyPreparedness/MedicalCountermeasures/UCM286201.pdf	The strategic plan describes FDA's strategic goals and key objectives through 2016 to build and sustain the programs needed to achieve the Medical Countermeasures Initiative mission. Medical countermeasures include drugs and biological products, medical devices, and other medical equipment that will be needed to protect the nation from public health emergencies involving chemical, biological, radiological, and nuclear threats, and emerging infectious diseases, such as pandemic influenza.
2012	DOI	*USGS National Wildlife Health Center, Strategic Science Plan: Advancing Wildlife and Ecosystem Health for the Next Decade* http://www.nwhc.usgs.gov/information_desk/NWHC%20Strategic%20Science%20Plan.pdf	This Plan describes how USGS will contribute to better protecting the Nation's natural resources from emerging disease threats through understanding of the causes and drivers of these emerging diseases and identification and understanding the underlying factors that enhance disease risks.
2012	Department of Defense (DOD)	*Medical Countermeasures Test and Evaluation Facility Final Report* News release (Medical Countermeasures Test and Evaluation Facility Final Report Results) http://mrmc.amedd.army.mil/index.cfm?pageid=media_resources.news_releases.MCM-TE_facility_refinement_study_results	This report forecasts the demand for an animal Biological Safety Level (BSL)-3 and BSL-4 medical countermeasures (MCM) test and evaluation (T&E) laboratory. The study assessed the existing capacity within government, industry, and academic laboratories to support this demand. Previous studies identified a significant gap that resulted in the concept for the MCM T&E Facility. Based on the most current findings of the study, the U.S. Army will not build a new MCM-T&E Facility but will expand T&E capability using current facilities. This decision will help close the research gap and meet the national demand to conduct MCM T&E in BSL-3 and BSL-4 laboratories. This report is in the process of being finalized.

2012	Department of Health and Human Services (HHS)	*Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy* https://www.medicalcountermeasures.gov/media/9035/2012-phemce-strategy.pdf and *PHEMCE Implementation Plan* https://www.medicalcountermeasures.gov/media/13962/2012-phemce-implementation-plan.pdf	The *2012 PHEMCE Strategy* builds on the 2007 Strategy and Implementation Plan to identify, create, develop, manufacture, and procure critical MCM. The *2012 PHEMCE Implementation Plan* describes the priorities that HHS, in collaboration with its interagency partners, will implement over the next five years to advance the strategic goals and underlying objectives established in the 2012 PHEMCE Strategy.
2012	OSTP/Department of Homeland Security (DHS)/U.S. Department of Agriculture (USDA)	Draft *2012-2016 R&D Plan for Foreign Animal Disease Threats (FADT)*	The Draft Plan updates the 2008 Plan and explores the R&D needs in the areas basic research, modeling, MCM development, and depopulation, decontamination, and disposal to enhance the Nation's ability to detect and respond quickly and effectively in the event of a foreign animal disease outbreak, whether naturally-occurring or intentionally-caused.
2012	Environmental Protection Agency (EPA)	*Wide-Area Response and Recovery Program (WARRP) Waste Management Workshop* http://www.epa.gov/wastes/homeland/docs/warrp_report.pdf	The workshop summary describes R&D needs (among other needs) to advance the planning and response of federal, state, and local officials in the area of waste management (segregation, temporary storage, transportation, treatment, and disposal) following a chemical, biological, or radiological (CBR) wide-area incident.
2012	USDA	*USDA Agricultural Research Service Capital Investment Strategy* http://www.ars.usda.gov/sp2UserFiles/Subsite/ARSLegisAffrs/USDA_ARS_Capital_Investment_Strategy_FINAL_eeo.pdf	This report establishes criteria and an enduring process for assessing and determining recurring capital investment needs, priorities and recommendations for USDA Agricultural Research Service scientific research laboratories, including biocontainment facilities based upon relative facility physical conditions and research program priorities.
2012	DHS	*The 2012 National Biodefense and Analysis Countermeasures Center*	The *NBACC Strategic Plan* establishes strategic goals that target a ten year planning horizon.

		(NBACC) Strategic Plan http://bnbi.org/about-us-2/strategic-plan/	
2012	HHS/National Institutes of Health (NIH)	*Final Supplementary Risk Assessment for the Boston University National Emerging Infectious Diseases Laboratories (NEIDL)* http://www.bu.edu/neidl/files/2013/01/SFEIR-Volume-III.pdf	The Risk Assessment presents the human health consequences of a potential accidental event or malevolent action resulting in the loss of pathogen or biological containment (biocontainment) at the Boston University Medical Center NEIDL.
2011	HHS/Office of the Assistant Secretary for Preparedness and Response (ASPR)	*BARDA Strategic Plan. 2011-2016* https://www.medicalcountermeasures.gov/media/745/bardastrategicplan9-28--508.pdf	The plan articulates the guiding principles, goals, and strategies that ASPR/BARDA will implement to enhance the capability of the U.S. Government to develop medical countermeasures (MCMs) to these and other natural and intentional threats to public health.
2011	DHS	*WARRP: Front-End Systems Engineering Study and Gap Analysis* (in the Wide Area Recovery and Resiliency Program (WARRP) Integrated Program Plan at: http://oai.dtic.mil/oai/oai?verb=getRecord&metadataPrefix=html&identifier=ADA580891)	The Study and Gap Analysis establishes a body of knowledge to inform federal, state, and local recovery capabilities. This effort includes the full breadth of study necessary to identify and prioritize gaps, align them with other national efforts, and to provide program leadership with the knowledge and situational awareness to support near, mid, and long-term investment decision making, as well as the national research agenda for improving long-term recovery from domestic chemical, biological, and radiological events.
2011	DHS	*The Strategic National Risk Assessment in Support of PPD 8: A Comprehensive Risk-Based Approach toward a Secure and Resilient Nation* http://www.dhs.gov/xlibrary/assets/rma-strategic-national-risk-assessment-ppd8.pdf	The Strategic National Risk Assessment evaluates the risk from known threats and hazards that have the potential to significantly impact the Nation's homeland security. These threats and hazards were grouped into a series of national-level events with the potential to test the Nation's preparedness.

2009	OSTP	*National Research and Development Strategy for Microbial Forensics* http://www.whitehouse.gov/files/documents/ostp/NSTC%20Reports/National%20MicroForensics%20R&DStrategy%202009%20UNLIMITED%20DISTRIBUTION.pdf	The Strategy and Implementation Plan focus the research efforts of the USG to advance the discipline of microbial forensics and provide the nation with the most scientifically sound and statistically defensible capability to provide scientific data to support attribution investigations of a potential or actual biological attack.
2009	DHS	*National Bio and Agro-Defense Facility (NBAF) Final Environmental Impact Statement* http://www.dhs.gov/environmental-impact-statement-process-nbaf	This environmental impact statement presents an evaluation of the DHS proposal to site, construct, and operate the NBAF. Operation of the NBAF as a BSL-3 and BSL-4 research facility would allow basic and advanced research, diagnostic testing and validation, countermeasure development, and diagnostic training for addressing high-consequence livestock diseases to U.S. agriculture and public health.
2009	EPA	*Five-Year Research and Development Roadmap for Wide Area Biological Restoration*	This roadmap establishes a desired 5-year end-state, including technologies, methods and policies that would greatly enhance wide area restoration capabilities and reduce restoration timelines, yet are reasonably achievable in the next 5 years. The roadmap also provides a research and development strategy, including science, technology and policy milestones, to achieve this desired 5-year end-state.
2008	HHS/NIH	*Blue Ribbon Panel to Advise on the Risk Assessment of the National Emerging Infectious Diseases Laboratories at Boston University Medical Center*	The Blue Ribbon Panel provided independent scientific advice on the supplementary risk assessment, including questions to be addressed, possible scenarios, specific infectious agents to consider as well as guidance on processes, methods, and modeling techniques that would result in a comprehensive, sound, and credible risk analysis.
2007	HHS	*PHEMCE Strategy and Implementation Plan for CBRN Threats* https://www.medicalcounte	The 2007 *PHEMCE Strategy and Implementation Plan* describe advanced development and acquisition priorities for CBRN MCM. These MCM address threats including anthrax, smallpox, botulism toxin, and radiological and nuclear agents. They will

		rmeasures.gov/barda/requirements-setting/hhs-phemce-strategy.aspx	allow HHS to better respond to public health emergencies caused by intentional threats or natural events, ultimately saving lives and reducing illness.
2007	HHS/NIH	Update to the *National Institute of Allergy and Infectious Diseases (NIAID) Strategic Plan for Biodefense Research* (http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Pages/strategicplan.aspx) http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/biosp2007.pdf	The *NIAID Strategic Plan for Biodefense Research* was published in 2002 and was followed by two research agendas, one for Category A agents and another for Category B and C priority pathogens. This updated Strategic Plan continues to focus on basic research and its application to product development, there is a shift from the current "one bug-one drug" approach toward a more flexible, broad spectrum approach.
2007	OSTP/DHS/ USDA	*Protecting Against High Consequence Animal Diseases: Research & Development Plan for 2008-2012* http://www.whitehouse.gov/sites/default/files/microsites/ostp/fadt_rd_16_feb_2007.pdf	This Plan establishes R&D requirements and priorities for FADs considered the greatest economic threat to the United States.
2006	HHS/NIH	*Progress Report for NIAID Biodefense Research Agenda for CDC Category A Agents* http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/cata_2006.pdf	This progress report describes the progress that has been made toward addressing the immediate goals outlined in the research agenda.
2003	OSTP	*OSTP Blue Ribbon Panel on the Threat of Biological Terrorism Directed Against Livestock* http://www.whitehouse.gov	OSTP tasked an international panel with representatives from National, state and local governments, academia, and industry with assessing the likelihood and potential consequences of biological terrorism directed against U.S. agricultural livestock, and recommending priorities for a federal defense

		/files/documents/ostp/NSTC%20Reports/2003%20Livestock%20Blue%20Ribbon.pdf	R&D agenda. The Blue Ribbon Panel identified research needs for specific prioritized diseases and noted that for Nipah and Hendra henipaviruses, due to their zoonotic potential, should stimulate consideration to the feasibility of constructing a BSL-4 facility with a significant large animal capacity to research existing and emergent highly contagious animal diseases.
2004	HHS/NIH	*Progress Report for NIAID Biodefense Research Agenda for Category B and C Priority Pathogens* http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/category_bc_progress_report.pdf	This progress report describes the progress that has been made toward addressing the immediate goals outlined in the research agenda.
2003	HHS/NIH	*Progress Report for NIAID Biodefense Research Agenda for CDC Category A Agents* http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/category_a_progress_report.pdf	This progress report describes the progress that has been made toward addressing the immediate goals outlined in the research agenda.
2003	HHS/NIH	*NIAID Biodefense Research Agenda for Category B and C Priority Pathogens* http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/categorybandc.pdf	This R&D agenda supports the 2002 Strategic Plan.
2002	HHS/NIH	*NIAID Strategic Plan for Biodefense Research* http://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/strategicplan.aspx	This Strategic Plan guides the implementation of a R&D agenda to support fundamental research on pathogens and the development of diagnostics, therapeutics, and vaccines. The *NIAID Biodefense Research Agenda for CDC Category A Agents* supports the 2002 Strategic Plan. The *Strategic Plan* was informed by recommendations from the NIH Blue Ribbon

		and *NIAID Biodefense Research Agenda for CDC Category A Agents* http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Documents/biotresearchagenda.pdf	Panel on Bioterrorism and Its Implications for Biomedical Research, that noted that achievement of the goals in the agenda to support fundamental research on pathogens and the development of diagnostics, therapeutics, and vaccines required the construction and certification of appropriate biocontainment facilities.
Non-Federal			
2012	NAS	*Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories* http://www.nap.edu/catalog/13315/biosecurity-challenges-of-the-global-expansion-of-highcontainment-biological-laboratories?version=b&utm_expid=4418042-5.krRTDpXJQISoXLpdo-1Ynw.1	This workshop report discusses the importance of implementing a needs assessment that precedes facility design and construction and involves all parties in the discussion.
2012	NAS	*Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options* http://www.nap.edu/catalog/13454/meeting-critical-laboratory-needs-for-animal-agriculture-examination-of-three#orgs	This National Academies of Science report discusses the laboratory infrastructure needed to effectively address the threat posed by animal and zoonotic diseases and analyzes three options for creating this infrastructure: building the National Bio- and Agro-Defense Facility (NBAF) as currently designed, building a scaled-back version of the NBAF, or maintaining current research capabilities at Plum Island Animal Disease Center (PIADC) while leveraging BSL-4 large animal capabilities at foreign laboratories.

APPENDIX F

National Bio and Agro-Defense Facility (NBAF)
Program Requirements – Historical Documentation

Date	Activity
August 2002	A biocontainment feasibility study was completed by Science Applications International Corporation (SAIC) for USDA that considered the possibility of conducting research and diagnostics of exotic diseases on the U.S. mainland, as well as operational cost issues regarding PIADC. This study cited the need for expanded capability, but raised concerns about the functionality and cost structure of PIADC infrastructure going forward. Concurrent with this study, SAIC performed a review that considered the national need, siting, operations, and programmatic support for a USDA BSL-4 research and diagnostic facility. This second study identified a void in our nation's ability to conduct large animal BSL-4 research, and the need for such a capability in developing countermeasures to high consequence zoonotic diseases. Together, both studies raised fundamental issues about the ability of the current PIADC infrastructure to meet our Nation's biosecurity needs.
November 2002	The Homeland Security Act of 2002 created DHS to protect against and respond to terrorist attacks within the United States. The Act transferred ownership of PIADC to DHS.
December 2003	The White House Office of Science and Technology Policy (OSTP) organized a Blue Ribbon Panel to examine research and development requirements and support efforts to mitigate the potential threat of bioterrorism directed against agricultural livestock. This panel presented a series of recommendations including a prioritization of pathogens requiring study [Kelly, 2003].
January 2004	Consultations between DHS and USDA regarding the coordinated agricultural research strategy, as called for in the Homeland Security Act of 2002 and Homeland Security Presidential Directive 9 (HSPD-9), "Defense of U.S. Agriculture and Food," January 30, 2004, revealed a capability gap in the development of new countermeasures against the introduction or natural occurrence of foreign animal and zoonotic diseases. HSPD-9 also specifically identified the need for "safe, secure, and state-of-the-art agriculture biocontainment laboratories that research and develop diagnostic capabilities for foreign animal and zoonotic diseases." To address the capability gap and need for modern biocontainment facilities, DHS is building the NBAF to conduct advanced research, diagnostic testing, and biologic countermeasure development for high-threat diseases affecting livestock.
October 2004	S&T prepared a report for *Congress titled A Comprehensive Strategy to Combat Agro Terrorism,* which described the threats to our nation and identified gaps in our research portfolio related to HSPD-9. Without the NBAF, the nation's livestock and food supply chain will be vulnerable to high consequence FADs and zoonotic diseases. A new facility must be developed that has the capacity to meet these demands.
July 2005	The DHS Joint Requirements Council validated the NBAF mission need and recommended initiation of conceptual design and award of the architecture and engineering (A&E) contract.

January 2006	DHS completed the Program Definition Document.
January 2006	DHS began the site selection process for NBAF by issuing an Expression of Interest for Potential Sites for NBAF as published in FedBizOpps.
May 2006	NBAF becomes a Level 1 Investment as part of the DHS acquisition process and was authorized to initiate planning.
January 2007	The Subcommittee on Foreign Animal Disease Threats, Committee on Homeland and National Security, National Science and Technology Council issues *Protecting Against High Consequence Animal Diseases: Research & Development Plan for 2008-2012*. This document provides a framework to meet HSPD-9 that reinforces the need for NBAF.
August 2007	The NBAF Feasibility Study is issued to explore the programmatic, technical, and non-site-specific requirements for NBAF in order to make a determination as to the feasibility of the project (given what is discovered) and the conceptual design (that is proposed) as a result of the efforts of this study.
July 2008	The Site Cost Analysis is developed to assess the estimated costs to construct NBAF at the potential site alternatives in the NBAF Environmental Impact Statement (EIS).
December 2008	The Final EIS is issued summarizing the potential impacts of construction and operating NBAF at the six site alternatives, which included Plum Island.
December 2008	The *World at Risk: The Report of the Commission on the Prevention of WMD Proliferation and Terrorism* is published and further underscores the potential biological threats that the U.S. may face.
January 2009	DHS selected the Manhattan, Kansas site to construct and operate NBAF. A Record of Decision was issued to document the basis of the decision.
June 2009	The NBAF Design Basis Threat Policy document identifies the most likely threats that must be addressed in the NBAF design for physical security.
August 2009	DHS completes the final Mission Needs Statement as part of the DHS acquisition process.
November 2009	The NBAF schematic design is completed.
January 2010	A Site-Specific Threat and Risk Assessment is completed that considered intentional acts against the NBAF.
October 2010	The Site-Specific Threat and Risk Assessment (SSRA), based on the 35% NBAF design documents, is issued and presented to the National Academy of Sciences (NAS) for review. The SSRA identified mitigation strategies for the design and operation of NBAF. All recommended enhancements were incorporated into the NBAF design.
February 2012	The Updated SSRA is issued and presented to NAS for review. This document confirmed that after the mitigation strategies recommended from the SSRA were incorporated into the NBAF design, there is a 'de minimis' chance of an outbreak caused by NBAF.
July 2012	The NAS Report *Meeting Critical Laboratory Needs for Animal Agriculture: Examination of Three Options* is issued. This report affirmed the need for an ABSL-4 and noted that PIADC is well past its prime, is expensive to maintain, and is isolated from academic and other research and development centers (which affects attracting high-level scientists), and that reliance on foreign laboratories and their priorities in times of need could leave the United States vulnerable.

July 2012	The NBAF design is completed.

Process Support Literature

- The Homeland Security Act of 2002 [PL 107-296, Title III, Section 302(4) and Section 308(c) (2)]
- OST 2004. The Office of Science and Technology Policy Blue Ribbon Panel on the Threat of Biological Terrorism Directed Against Livestock.
- HSPD 2004, Homeland Security Presidential Directive / HSPD-9, Subject: Defense of United States Agriculture and Food.
- NRC. 2005. Critical Needs for Research in Veterinary Science. Washington DC: The National Academies Press.
- October 21, 2009. THE CLOCK IS TICKING: A Progress Report on America's Preparedness to Prevent Weapons of Mass Destruction Proliferation and Terrorism
- 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.
- Federal Register. 2009. Record of Decision for the NBAF Environmental Impact Statement. US Department of Homeland Security, Science and Technology Directorate. Washington DC: US Government Printing Office. 74(11):3065-3080 [online]
- 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. 2010. Site-Specific Biosafety and Biosecurity Mitigation Risk Assessment. Final Report, Vol. 1, October 2010 [online]. Available: http://www.dhs.gov/xlibrary/assets/nbaf_ssra_final_report.pdf. 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_executive_summary.pdf. NRC (National Research Council). 2012. Meeting Critical Laboratory Needs for Animal Agriculture. Washington DC: The National Academies Press

NAS/NRC/IOM

- World Bank. People, Pathogens and Our Planet. Volume 1: Towards a One Health Approach for Controlling Zoonotic Diseases. Report No. 50833-GLB. Washington, D.C. 2010.
- IOM and NRC. 2009. Sustaining global surveillance and response to emerging zoonotic diseases, 312 pages. Gerald T. Keusch, Marguerite Pappaioanou, Mila C. González, Kimberly A. Scott, and Peggy Tsai (Eds.), Committee on Achieving Sustainable Global Capacity for Surveillance and Response to Emerging Diseases of Zoonotic Origin; The National Academy Press, Washington, D.C.
- Beatty, A., K. Scott, and P. Tsai. 2008. Achieving sustainable global capacity for surveillance and response to emerging diseases of zoonotic origin: Workshop summary. Committee on achieving sustainable global capacity for surveillance and response to emerging diseases of zoonotic origin, National Research Council.

- IOM and NRC. 2002. The Emergence of Zoonotic Diseases: Understanding the Impact on Animal and Human Health - Workshop Summary, 176 pages. Tom Burroughs, Stacey Knobler, and Joshua Lederberg, (Eds.), Forum on Emerging Infections, Board on Global Health; The National Academy Press, Washington, D.C.
- IOM. 2003. Microbial threats to health: Emergence, detection and response, 367 pages. Mark S. Smolinski, Margaret A. Hamburg, and Joshua Lederberg (Eds.), Committee on Emerging Microbial Threats to Health in the 21st Century. The National Academy Press, Washington, D.C.
- IOM. 2006. Addressing foodborne threats to health. Policies, practices and global coordination, 304 pages. Workshop summary, Forum on Microbial Threats and Board of Global Health. National Academies Press, Washington, D.C.
- National Research Council. 2005. Animal health at the crossroads- Preventing, detecting and diagnosing animal diseases, 286 pages. Committee on Assessing the Nation's Framework for Addressing Animal Diseases. Board on Agriculture and Natural Resources. The National Academies Press, Washington, D.C.
- National Research Council. 2005. Critical needs for research in veterinary science, 222 pages. Committee on the National Needs for Research in Veterinary Science. National Academies Press, Washington, D.C.
- IOM 2010. Rapporteur's Workshop Summary: Infectious Disease Movement in a Borderless World. Relman, DA, Choffnes, ER and Mack A. Forum on Microbial Threats and Board of Global Health. National Academies Press, Washington, D.C.
- IOM 2012. Rapporteur's Workshop Summary: Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories. Hottes. AK, Rusek B, Sharples F. Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories. Committee on International Security and Arms Control Policy and Global Affairs Division. Board on Life Sciences. Division on Earth and Life Studies. National Academies Press, Washington, D.C.
- Bram, R.A., J.E. George, R.E. Reichard and W.J. Tabachnick. 2002. Threat of Foreign Arthropod-Borne Pathogens to Livestock in the United States. J. Med. Entomol. 39(3):405-416.

USDA

- Blayney D.P., J. Dyck J., and D. Harvey. Economic effects of animal diseases linked to trade dependency. USDA. Economic Research Service, April 2006.
- Paarlberg, PL, Seitzinger AH, Lee HG, and KH Mathews. Economic Impacts of Foreign Animal Disease. USDA. Economic Research Service, May 2008.
- Office of Risk Analysis and Cost Benefit Analysis, Office of the Chief Economist (USDA). Economic impact of a foreign animal disease (FAD) outbreak across the United States. Washington, D.C. June 16, 2005.

Agroterrorism

- Kelly, T., P. Chalk, J. Bonomo, J. Parachini, B.A. Jackson and G. Cecchine. The Office of Science and Technology Policy Blue Ribbon Panel on the Threat of biological terrorism directed against livestock, CF-193-OSTP, April 2004.

- PL 107-9 Federal Inter-agency Working Group. Animal disease risk assessment, prevention and control act of 2001 (P.L. 107-9): Final Report of the P.L. 107-9 Federal Inter-Agency Working Group. January 2003.
- Parker, Henry. Agricultural Bioterrorism: A Federal Strategy to Meet the Threat. McNair Paper 65. National Defense University. Washington, D.C. 2002.
- Gronvall, GK and Bouri, N. 2008. Biosafety Laboratories. Biosecurity and Bioterrrorism: Biodefense Strategy, Practice and Science Vol. 6, No 4.
- Chalk, Peter. Hitting America's soft underbelly: the potential threat of deliberate biological attacks against the U.S. agriculture and food industry. A Report for the Office of the Secretary of Defense. RAND National Defense Research Institute. 2004.
- Crutchley, T.M., J.B. Rodgers, H.P. Whiteside Jr., M. Vanier and T.E. Terndrup. 2007. Agroterrorism: Where are we in the ongoing war on terrorism? J. Food Protection 70(3):791-804.
- Gewin, V. 2003. Agriculture shock. Nature 421:106-8.
- Casagrande, R. 2002. Biological Warfare Targeted at Livestock. BioScience 52(7):577-581.
- Wheelis, M., R. Casagrande and L. Madden. 2002. Biological Attack on Agriculture: Low-Tech, High-Impact Bioterrorism BioScience 52(7):569-576
- Hugh-Jones, M. and C.C. Brown. 2006 Accidental and intentional animal disease outbreaks: assessing the risk and preparing an effective response. Rev. Sci. Tech. 25(1):21-33.

Tab D

Fast Track Action Committee Report:

Recommendations on the Select Agent Regulations Based on Broad Stakeholder Engagement

October 2015

National Science and Technology Council

Committee on Homeland and National Security

Subcommittee on Biological Defense Research and Development

Fast Track Action Committee on the Select Agents Regulations

Executive Summary

Following several biosafety incidents at U.S. Government laboratories in 2014, the White House issued a memorandum outlining a series of short- and long-term actions to enhance laboratory biosafety and biosecurity practices.

One short-term action was a safety stand-down for all Federal laboratories that possess, use, or transfer human, animal, or plant infectious agents or toxins. Senior leadership and staff of departments and agencies were urged to review and improve biosafety and biosecurity practices, as needed. Departments and agencies were also urged to develop and implement plans for a sustainable inventory management and control system. Long-term actions included engaging broader stakeholders' input into how the Select Agent Regulations (SAR) have impacted science, technology, and national security in the United States.

In order to engage a wide range of stakeholders, the National Science and Technology Council (NSTC) established a Fast Track Action Committee (FTAC) on the Select Agent Regulations under the Subcommittee on Biological Defense Research and Development of its Committee on Homeland and National Security. The FTAC and the White House Office of Science and Technology Policy (OSTP) convened two listening sessions of SAR stakeholders to provide individual views to inform and support the process. Furthermore, the FTAC published a Request for Public Comment in the Federal Register to collect additional input from interested individuals and organizations throughout the United States and globally.

This report describes findings and recommendations formulated from the listening sessions, the responses to the Federal Register notice, and previous reviews of the SAR. Recommendations from stakeholders obtained during the information gathering process focused on ways to improve the regulatory process and address perceived gaps in the SAR in the future. Based on individual stakeholder input, the FTAC developed recommendations that it believes can be reasonably implemented. The FTAC also identified more complex issues that will require additional analysis before specific proposals can be developed and evaluated.

FTAC Recommendations

1. Regulation Interpretations: The FTAC recommends developing a formal mechanism for issuing, publicizing, and accepting requests for interpretations of the SAR.

2. Public Release of Information: The FTAC recommends that information about biological select agents and toxins (BSAT) research, including laboratory incidents, be periodically provided to the public, and that Federal BSAT laboratories adopt, to the maximum extent feasible, a policy of transparency regarding both the agents used and laboratory incidents.
3. Sharing Best Practices: The FTAC recommends members of the regulated community establish a mechanism for sharing best practices.
4. Individual-based Security Risk Assessments: The FTAC recommends that in the absence of specific information indicating otherwise, individuals who have been granted access to select agents or toxins at one BSAT institution be able to move to another BSAT institution without having to wait for a new Security Risk Assessment.
5. Emergency Situations: The FTAC recommends development of a mechanism to expedite approvals or to relax Federal Select Agent Program (FSAP) requirements in response to time-urgent emergency situations.
6. Inventory Control Requirements: The FTAC recommends retaining requirements to maintain inventories of samples containing biological select agents and toxins, while ensuring that BSAT institutions are not requested to characterize biological agents quantitatively.
7. Consistency of Inspections: The FTAC recommends development of an approach to improve the consistency of the inspection process across inspectors, inspecting agencies, and inspected sites.
8. Improve Customer Service in Communicating with Regulated Entities: The FTAC recommends improving communication before and after site inspections and improving the timeliness of inspection reports.
9. Categorize Inspection Findings: The FTAC recommends developing a system to categorize findings on inspection reports.
10. Appeals Process: The FTAC recommends expanding the appeals process for institutions to adjudicate disputed findings in inspection reports.
11. Peer Advisory Mechanism: The FTAC recommends creating an expert panel or Federal Advisory Committee to serve as an external group that could share best practices or make recommendations to the FSAP.
12. International Engagement: The FTAC recommends international engagement to explore harmonization of pathogen security standards and ensure understanding of the rationale for, and implementation of, the SAR-equivalent standards by collaborating foreign governments.

13. Guidance for Customs Inspectors: The FTAC recommends providing better training and guidance for customs inspectors who process BSAT shipments.

Issues for Further Analysis

A. Institutional Scope of Regulation: Consider whether to bring all bioscience institutions, or at least all those operating at or above Biosafety Level 3 or "high containment", under Federal biosafety regulation.

B. Possible Exemptions for Quality Assurance: Consider creating exemptions from certain security regulations for laboratories that retain certain select agents only for the purposes of positive control material availability and quality-assurance procedures.

C. Security Expenses: Examine mechanisms for funding security-related expenses for use of BSAT; determine if those mechanisms are adequate; and if not, propose options to ensure that funding is available for necessary security measures.

D. Consistent Disclosure Policies: Seek to ensure that institutions regulated under the SAR fall under consistent information-disclosure policies, to the extent that State and local laws and regulations pertaining to these institutions can be reconciled with Federal requirements.

E. Common Chemical, Biological, and Radiological Security Framework: Explore the feasibility of establishing a common interface for institutions—with respect to personnel vetting and personnel reliability—for people with access to chemical, biological, and radiological materials of security concern.

F. Risk-based Approach: Explore the feasibility of adopting a "risk-based" approach to managing the safety and security oversight of biological agents and toxins.

G. Shipping Regulations: Review domestic and international shipping regulations and requirements, as well as related guidance, with a view to simplifying and clarifying, and to facilitating compliance by other countries.

Contents

A. Introduction

Life sciences research in the United States is essential to characterize, prevent, detect, and respond to biological threats of natural, accidental, or deliberate origin. It is the U.S. Government's responsibility to ensure that life sciences research in the United States is conducted safely and securely. In the summer of 2014, laboratory biosafety/biosecurity incidents in U.S. Government facilities led Lisa O. Monaco, the Assistant to the President for Homeland Security and Counterterrorism, and John P. Holdren, the Assistant to the President for Science and Technology, to issue a memorandum outlining a series of immediate and longer-term steps the U.S. Government would take to identify and address the underlying causes of these incidents.[1]

Issued August 18, 2014, the memorandum urged all U.S. Government departments and agencies that operate facilities that possess, use, or transfer *any* human, animal, or plant infectious agent or toxin to perform a safety stand-down. The memo also urged all such departments and agencies to prepare an immediate full accounting of their holdings to (1) identify any biological select agents and toxins and ensure their proper registration, safe stewardship, and secure storage or disposal; and (2) have senior leaders devote time to review laboratory biosafety and biosecurity best practices and protocols and develop a sustainable inventory monitoring plan. The memorandum also urged non-federal and international entities that receive Federal Government funds to voluntarily take part in similar activities.

The longer-term actions included reconvening the Federal Experts Security Advisory Panel (FESAP, established in 2010 by Executive Order 13546) to conduct a coordinated Federal review to identify gaps and make recommendations for optimizing biosafety, biosecurity, oversight, and inventory management and control of biological select agents and toxins.[2] They also included the formation of an interagency group to comprehensively engage the broader stakeholder community to review the impact that the Select Agent Regulations[3] (SAR) have had on science, technology, and national security. This second action was to ensure that members of the scientific, regulatory, and security communities, as well as interested citizens, would have an opportunity to provide direct feedback on this important issue.

---

[1] L. Monaco, and J. Holdren, "Ensuring Biosafety and Biosecurity in U.S. Laboratories,"*https://www.whitehouse.gov/sites/default/files/microsites/ostp/enhancing_biosafety_and_biosecurity_19aug2014_final.pdf.*

[2] Executive Order 13546, "Optimizing the Security of Biological Select Agents and Toxins in the United States," July 2, 2010, https://www.whitehouse.gov/the-press-office/executive-order-optimizing-security-biological-select-agents-and-toxins-united-stat.

[3] 42 CFR Part 73, 9 CFR Part 121, 7 CFR Part 331.

To ensure that this stakeholder review benefited from diverse perspectives and the broadest possible input, the National Science and Technology Council established a Fast Track Action Committee (FTAC) on the Select Agent Regulations under the Subcommittee on Biological Defense Research and Development of its Committee on Homeland and National Security. The FTAC and the White House Office of Science and Technology Policy (OSTP) convened two listening sessions of SAR stakeholders (February 17, 2015, and March 20, 2015) to inform the process and provide insight into how the SAR have affected science, innovation, biosafety, and biosecurity in the United States. Approximately 55 individual scientists, research administrators, biosecurity experts, and other interested stakeholders attended the two sessions, either in person or by teleconference. The specific goals of the listening sessions were to solicit a broader and deeper understanding of the impact of the SAR on science and innovation, safety and security, and public or agricultural health and response, as well as understand how the SAR might be applied now and in the future. Appendix A summarizes the individual comments provided at the meetings.

On March 16, 2015, the FTAC published a Request for Public Comment in the Federal Register to collect additional input from interested individuals and organizations throughout the United States and globally regarding the impacts of the SAR on science, technology, biosafety, and biosecurity.[4] During the three-week comment period, 43 submissions from 63 respondents were received. The perspectives, observations, and recommendations gathered from the listening sessions and the Federal Register submissions coalesced around a few overall themes. Including the listening sessions, a total of 118 stakeholders provided comments on both negative and positive impacts of the SAR, on specific challenges related to SAR implementation, and on perceived gaps in the SAR as currently conceived and implemented. Recommendations received during the information-gathering process focused on ways to improve the regulatory process and address gaps in the SAR in the future. The FTAC reviewed the recommendations it received, grouping them by topic.

Section B of this report provides general background on the SAR. Section C is a summary of general comments and observations. Section D contains the most salient and actionable FTAC recommendations based on stakeholder feedback. Finally, the more complex issues, including those that require more analysis than is feasible under the FTAC's timeline, are presented in Section E.

[4] Impact of the Select Agent Regulations, Federal Register Notice (80 FR 13639), March 16, 2015, https://www.federalregister.gov/articles/2015/03/16/2015-05906/impact-of-the-select-agent-regulations.

B. Background and Previous Reports on Biosafety and Biosecurity

The SAR were developed so that the U.S. Government could minimize the risk of bioterrorism and ensure the legitimate use of pathogens by regulating the security and safety of entities that possess, transfer, or use certain (select) biological pathogens and toxins. Title V of Public Law 104-132 (1996) included provisions that required the Secretary of Health and Human Services (HHS) to regulate the transfer of select agents and toxins from one laboratory to another.[5] This authority was expanded to cover possession and utilization of these agents by Public Law 107-188.[6] Public Law 107-188 authorizes the Secretaries of Health and Human Services and Agriculture to regulate the possession, use, or transfer of a "select" list of human, animal or plant infectious agents or biological toxins (biological select agents or toxins, or BSAT) that have the potential to pose a severe threat to public, animal, or plant health or animal and plant products. Public Law 107-188 requires a biennial review of the BSAT list during which BSAT may be added or removed based on new information or a better understanding of the risks they pose.

The SAR require individuals, private and public organizations, academic institutions, and government agencies in the United States to register with the Federal Select Agent Program (FSAP) before they can lawfully possess and use BSAT. Implementation of these regulations is delegated to the Centers for Disease Control and Prevention's (CDC) Division of Select Agents and Toxins (DSAT) for HHS and to the Animal and Plant Health Inspection Service's (APHIS) Agriculture Select Agent Services (AgSAS) for the United States Department of Agriculture (USDA). DSAT and AgSAS operate as the FSAP to coordinate the regulation of BSAT. Between 2004 and 2010, over 300 entities registered to possess, use, or transfer BSAT, and more than 13,171 individuals (scientists, technicians, and support personnel) were approved for access to select agents.[7] In 2012, the SAR were modified to create two tiers of BSAT. Fifteen agents and toxins posing the greatest risk were designated as "Tier 1" agents, and additional regulations were imposed upon institutions possessing and working with them. These regulations included requirements for occupational health and personnel suitability assessments for staff with access to or who work with Tier 1 select agents.

---

[5] Antiterrorism and Effective Death Penalty Act of 1996, Public Law 104-132, April 24, 1996, http://www.gpo.gov/fdsys/pkg/PLAW-104publ132/pdf/PLAW-104publ132.pdf.

[6] Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188 Sec. 231, June 12, 2002, http://www.gpo.gov/fdsys/pkg/PLAW-107publ188/pdf/PLAW-107publ188.pdf.

[7] R. D. Henkel, T. Miller, and R. S. Weyant, "Monitoring Select Agent Theft, Loss and Release Reports in the United States—2004–2010," *Appl. Biosafety* 17 (2012), 171–180.

There have been multiple, complementary, and sometimes overlapping efforts, both Federal and non-federal, to scrutinize and evaluate the issues related to BSAT, personnel and cyber security, FSAP administration, and the benefits and costs of SAR implementation.[8] These previous efforts include reports from a number of Federal task forces and panels that can be found on the Legal Authorities, Policies and Committees page of the Public Health Emergency, Department of Health and Human Services website: the Executive Order 13486 Working Group on Strengthening the Biosecurity of the United States (2009) report, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (TFTF) report (2009), and the report of the Federal Experts Security Advisory Panel (2010).[9]

The FTAC's review of these reports was not exhaustive, but rather weaves together the many threads and recommendations of previous efforts pertinent to the purpose of this FTAC. The FTAC also drew upon a number of non-federal reviews that echoed many of the issues identified and reiterated in this FTAC report. For example, while greater transparency is a continuous theme in these reports, it also stands out as a continuous challenge for all parties. Greater transparency was a key recommendation from the TFTF and FESAP reports, as well as reports from the National Science Advisory Board on Biosecurity (NSABB),[10] the National Science Foundation, Institute of Medicine advisory groups, professional societies and the broader community. These reports highlight the important role that communication and information sharing with communities that surround high-level containment laboratories play in good-neighbor relationships and in fostering a culture of transparency. Also highlighted were the cost of effective biosecurity, personnel suitability requirements, standardized and harmonized approaches to site inspections, inventory systems, and collaborative problem-solving.

C. Stakeholder Comments and Observations

This broad stakeholder engagement on the review of the impact of SAR on science, technology, and national security draws on an extensive background of previous studies of the SAR regulations and FSAP program. The FTAC has arrived at a number of recommendations that it believes can be reasonably implemented. It also highlighted more

---

[8] S. A. Morse, "Pathogen Security—Help or Hindrance?" *Frontiers in Bioengineering and Biotechnology* 2 (2015), 1–12.

[9] Public Health Emergency, Science Safety Security, Strategies and Reports, http://www.phe.gov/s3/strategies/Pages/default.aspx.

[10] National Science Advisory Board for Biosecurity, "Enhancing Personnel Reliability among Individuals with Access to Select Agents," May 2009, http://osp.od.nih.gov/sites/default/files/resources/NSABB%20Final%20Report%20on%20PR%205-29-09.pdf; National Science Advisory Board on Biosecurity, "Guidance for Enhancing Personnel Reliability and Strengthening the Culture of Responsibility," September 2011, http://osp.od.nih.gov/sites/default/files/resources/CRWG_Report_final.pdf.

complex, which will require additional analysis before specific proposals can be developed and evaluated.

The predominant sentiment of stakeholders is best captured in the statement by more than one individual that there is a "love-hate" relationship between the select agent-regulated community and the SAR as currently designed and implemented. Several stakeholders expressed the view that there were positive benefits to having oversight and inspections, particularly with respect to biosafety, that would not otherwise occur in the absence of the SAR. Since the SAR emphasize laboratory safety and require inspections, stakeholders expressed their belief that the SAR provide an extra impetus for laboratory personnel to be more diligent in working with select agents. Stakeholders also recognize that the SAR have helped prevent the unauthorized release of select agents and enhanced a culture of safety.

Stakeholders offered mixed perspectives on BSAT inventory accountability requirements; most of them viewed overall accountability requirements to be valuable and appropriate at the strategic level. There were also several specific and ardent concerns about the negative effects of the SAR, however, notably in terms of their impact on the willingness of researchers to work on BSAT, the financial costs of compliance, and the destruction of potentially valuable material as a result of inventory requirements.

1. Human Resources Costs

Many stakeholders said that the requirements of the SAR, particularly for Tier 1 agents, have become so financially and administratively burdensome that students, postdoctoral researchers, and well-established researchers are leaving research with BSAT in favor of research with non-select agents, although no data were provided. The majority of stakeholders who spoke on this issue implied that the overall strength of scientific advancement in select agent research in the United States is directly tied to the number of facilities and researchers working in the field. They also noted that researchers may in some cases be driven to perform research in countries that do not have the same regulatory requirements.

2. Financial Costs

Stakeholders suggested that the financial cost of physical security requirements and personnel suitability regulations around Tier 1 agents is a substantial burden to many institutions. Some said that several manufacturers have decided to stop producing veterinary vaccines or diagnostics due to a combination of rising SAR compliance costs and small profit margins for those products, which could affect the availability of products for agricultural health and emergency response. Following the establishment of the Tier 1 designation for 15 select agents and toxins, and the associated regulations, some institutions decided to abandon research with Tier 1 select agents because the financial

costs associated with compliance were too high. Stakeholders noted that implementing the SAR requires committing much time and money, especially for inventory control and staff to handle paperwork and ensure compliance. Several stakeholders said that they had at least one full-time equivalent employee devoted to SAR compliance, with many other individuals involved secondarily.

Additional topics discussed during the listening sessions included the negative impacts of the SAR on the food safety/manufacturing/processing industry, particularly with respect to botulinum neurotoxin's designation as a Tier 1 toxin. According to stakeholders, the cost of implementing Tier 1 regulations has led at least some food processors and manufacturers to cease their work with Tier 1 agents, which could have negative consequences for a public health emergency response involving the food supply.

3. Challenges with Personnel Suitability Requirements

Difficulties in implementing personnel suitability requirements for Tier 1 agents were noted, and some stakeholders said these requirements negatively affect their ability to engage highly qualified scientists. Several stakeholders noted that implementation of the SAR created particular burdens on public health laboratories, and in some cases, the lack of available security risk assessment "cleared" personnel could have a negative impact on responsive patient care by delaying testing of clinical samples. Multiple stakeholders in the listening session and in the Federal Register notice submissions suggested the need for better guidance or a mechanism for sharing and harmonizing best practices on the implementation of personnel suitability programs.

4. Gaps in the Select Agent Regulations

Some respondents believed that the potential risks posed by novel organisms and new techniques are significant and inadequately addressed by existing regulatory approaches. The rapid pace of advances in genetic engineering and molecular biology has lowered barriers to the ability of researchers to use recombinant technologies to potentially increase an organism's virulence or synthesize a biological select agent *de novo*. The ability to translate biological data into digital form and back again raises questions about regulatory oversight measures, such as the SAR, that rely on the physical presence of a pathogen. It was argued that additional consideration should therefore be given to regulatory approaches that anticipate technological challenges and are flexible enough to keep pace with them.

5. Consistency, Clarity, and Responsiveness of the Select Agent Program

Many stakeholders said a number of improvements were needed in how the SAR was implemented with regard to coordination between Federal regulatory agencies and the regulated community. One key comment was that the perceived lack of consistency in

interpretations of the SAR between regulatory agencies led to variations in application during rounds of inspections and even differences in interpretation between inspectors when conducting an inspection. Respondents also noted that a lack of communication about the scope and process of an inspection beforehand and delays in receiving responses from regulatory agencies about inquiries regarding inspection findings prevented SAR facilities from implementing compliance actions in time for the next inspection. Also, delays in approvals for specific research projects caused researchers to miss funding deadlines. Finally, protracted communications and ambiguities in the inspection process have resulted in more time spent in inspection preparation and compliance, an additional resource burden that is placed on SAR researchers. The FTAC recognized these concerns as "customer service" issues on the part of the FSAP and has offered recommendations to address them.

6. SAR in an International Context

A set of comments centered on considerations of the SAR and its impact on international engagement. Many stakeholders were concerned that restrictions placed on BSAT researchers in the United States would lead them to join foreign laboratories with more lenient requirements, in turn creating an unequal playing field. Moreover, stakeholders commented that a lack of clarity and understanding of the rationale and processes of the SAR by foreign researchers hinders international research relationships. Finally, stakeholders said they needed additional guidance on how the SAR affects their international research collaborations, as well as additional training for customs officials in handling international shipments of BSAT materials.

D. FTAC Recommendations

The FTAC recommendations are based on input gathered from two listening sessions and responses to a solicitation published in the Federal Register asking for comment on how the SAR have affected science, innovation, biosafety, and biosecurity in the United States.

1. Regulation Interpretations: The FTAC recommends developing a formal mechanism for issuing, publicizing, and accepting requests for interpretations of the SAR.

No regulations can be detailed enough to specify how they should be applied in every situation, particularly when—like the SAR—they are applied to a diverse set of institutions (e.g., clinical laboratories, academic research laboratories, public health laboratories, food manufacturing facilities, and animal facilities). The necessary provision of flexibility for case-by-case application introduces the possibility that the regulations may be interpreted in different ways by different institutions and by the officials who inspect them.

To minimize inconsistent interpretations of the regulations, several respondents have asked that a mechanism be established by which they can request a formal interpretation of the SAR as they apply to that institution's particular circumstance. Public issuance of an interpretation would provide predictability for the institution, minimize inconsistent interpretations by different inspectors, and allow other institutions in similar circumstances to adopt a consistent approach. The FTAC recommends the development of a formal mechanism for accepting requests for, issuing, publicizing, and holding consistently to interpretations of its regulations. However, given that application of the regulations can be site-specific and can depend on factors that would be difficult to capture in a statement of interpretation, there may be limitations on how effectively an archive of regulatory interpretations could serve to promote consistency in inspections across different institutions.

2. Public Release of Information: The FTAC recommends that information about BSAT research, including laboratory incidents, be periodically provided to the public, and that Federal BSAT laboratories adopt, to the maximum extent feasible, a policy of transparency regarding both the agents used and laboratory incidents.

Maintenance of the public trust is essential for conducting high- or maximum-containment biological research. This trust is enhanced when communities surrounding containment laboratories are confident that they are being kept aware of activities within the laboratories, including, but not limited to, the occurrence of incidents that might affect them. At the same time, the willingness of laboratories to provide such information is enhanced when there is confidence that such transparency will not prove harmful to them—for example, when the press and public clearly understand that multiple layers of protection stand between potentially hazardous pathogens and the public. Administrative irregularities or incidents involving a single one of these protective measures do need to be addressed, but by themselves do not necessarily put the public at risk.

News reports on incidents at biocontainment laboratories, as well as congressional testimony from interested parties and reports from the Government Accountability Office, have stressed the perceived opaqueness of the program. For example, one recent article asserted, "select agent oversight is cloaked in secrecy, making it difficult to assess regulators' effectiveness in ensuring safety." The article also quoted a member of a citizen advisory panel as saying, "the more people in the community [surrounding a select agent

research laboratory] feel that there's secrecy, the more they're distrustful, whether their distrust is warranted or not."[11]

The FTAC recommends that information about BSAT research or incidents in BSAT laboratories be shared with the public, to the maximum extent possible. In most cases, withholding this information has negligible security value, since the research, researchers, institutions, and agents involved with BSAT research are often published in scientific journals or can readily be inferred from public materials. However, the FTAC also recognizes that in many cases, certain work with BSAT, including work on the characterization of biological threats or the evaluation of their use in bioterror and biocrime events, cannot be fully released for security reasons, lest that information be used to facilitate the efforts of those who would seek to inflict harm with BSAT.

Specific statutory restrictions[12] preventing the Federal government from releasing certain select agent information in response to requests under the Freedom of Information Act do not preclude research institutions or government laboratories from voluntarily disclosing such information. Indeed, the biocontainment laboratories at Fort Detrick, Maryland, and Galveston, Texas, have started posting information about all their laboratory incidents on public websites. For example, Galveston National Laboratory provides the public with a history of possible exposures from 2002 to the present, including the name of the agent or toxin and a description of the incident.

Over time, providing biosafety data to the public will facilitate long-term risk assessments, provide the public with greater context for high-profile or novel events, and allow for assessment of the overall risk associated with biocontainment laboratories. Dissemination of this information, perhaps through a third-party professional organization, could mitigate concerns or direct needed resources, as appropriate. The FTAC recommends that institutions conducting BSAT research periodically, to the maximum extent possible, release information regarding their BSAT research programs and that the FSAP release aggregated information on laboratory incidents on an annual basis. The FTAC further recommends that the Federal Government lead by example and that Federal BSAT laboratories adopt, to the maximum extent feasible, a policy of transparency regarding both the agents used and laboratory incidents.

---

[11] See Alison Young and Nick Penzenstadler, "Inside America's Secretive Biolabs," *USA Today*, May 28, 2015, http://www.usatoday.com/story/news/2015/05/28/biolabs-pathogens-location-incidents/26587505/.

[12] See 42 USC 262a(h)(1).

3. Sharing Best Practices: The FTAC recommends members of the regulated community establish a mechanism for sharing best practices.

Listening session participants said that they would appreciate the opportunity to improve their safety and security practices by learning from their peers. Mechanisms to accomplish sharing best practices, such as a website, would be well received and would enhance safety and security among many institutions. The FTAC recommends establishing such an information-sharing mechanism, while recognizing that the FSAP might not be the best party to establish it. This need might best be met if the regulated institutions themselves, or a non-governmental entity such a professional society, were to establish a mechanism to do so and update the information in a timely manner.

FSAP sponsorship of such an information-sharing mechanism might put the program in the position of appearing to endorse a particular practice described there, which some institutions may find valuable, but which would not necessarily be researched or vetted by the FSAP. Moreover, government sponsorship may make it difficult to maintain a robust and frank dialogue among the participants in such an exchange, if that privacy were sought.

4. Individual-based Security Risk Assessments: The FTAC recommends that in the absence of specific information indicating otherwise, individuals who have been granted access to select agents or toxins at one BSAT institution be able to move to another BSAT institution without having to wait for a new Security Risk Assessment.

Once an individual undergoes a Security Risk Assessment and is permitted to work with select agents, any change to the list of agents he or she is working with, or a transfer to a different institution, should continue to require notification to FSAP. However, an individual transferring from one registered entity to another registered entity should not have to wait for the completion of a new Security Risk Assessment. This continued approval would be dependent on both the original institution and the receiving institution (1) formally exercising their responsibilities to report to the FSAP if an individual becomes a "restricted person," (2) being held accountable for their own personnel suitability assessments (meaning that the receiving institution needs to do its own if the individual will be working with Tier 1 agents), and (3) reporting suspicious behavior as required by the regulations. The FSAP would be able to update or redo the Security Risk Assessment at its discretion, and it always has the responsibility to deny access of the individual to select agents and toxins should disqualifying information be uncovered. However, the individual's access to select agents should be maintained without break, pending any such reevaluation. Notification of the change to FSAP would enable FSAP to conduct a new Security Risk Assessment if necessary, and maintain a current list of personnel who have access to select agents (including which agents they have access to and at which institutions), while minimizing unnecessary delays or duplicative investigations.

5. Emergency Situations: The FTAC recommends development of a mechanism to expedite approvals or to relax FSAP requirements in response to time-urgent emergency situations.

Some respondents noted that the development of a vaccine to an emerging pandemic strain of influenza would be impeded by the requirement to treat potential vaccine strains as select agents until the extensive process needed to show that they were attenuated. These respondents argued that highly pathogenic H5N1 avian influenza can be predictably attenuated by standard genetic methods used in vaccine development, making extensive testing unnecessary. If subject-matter experts are able to provide evidence of the efficacy of such attenuation methods through scientific documentation and peer-reviewed publications, the FSAP should evaluate whether employing such attenuation is sufficient to consider H5N1 influenza vaccine strains, or other influenza strains, as exempt from select agent controls. FSAP should also consider whether the exigencies of an emerging pandemic might warrant such a determination even if it might not be considered appropriate under normal circumstances.

Other FSAP requirements, such as the security provisions that prevent unauthorized individuals from gaining access to or working with select agents, would have less relevance during a widespread outbreak—during which patients, clinical samples, health-care environments, and other settings may be rife with the organism responsible—than they would have if the organism was strictly confined to approved laboratories. The FSAP program should be able to allow appropriate officials to expedite approvals or relax FSAP requirements in time-urgent emergency situations if those requirements are judged to confer negligible security value during an outbreak but would impede the response. (Note that relaxing or waiving safety requirements may not be appropriate, unless safety can be assured in the absence of experimental validation.) Any waived provisions could be reinstituted once the outbreak has been controlled.

The Secretaries of Health and Human Services and Agriculture already have authority to temporarily exempt individuals from the requirements of the SAR for the purpose of responding to domestic or foreign public health emergencies that involve select agents or toxins.[13] The FTAC recommends that the need for any additional waivers or waiver processes be examined, such as whether waivers are needed that are defined in terms of regulated actions, rather than actors; whether officials other than the Cabinet Secretaries should be able to issue them, and whether the emergencies that might prompt such waivers are sufficiently anticipated and defined in advance. If needed, these waivers should be provided for a defined time period, or for as long as some pre-defined set of conditions are satisfied, with the option to review for an extension.

[13] See 42 USC 262a(g)(3) and (4); 7 USC 8401(g)(1)(D) and (E); and 7 USC 8401(g)(2).

6. Inventory Control Requirements: The FTAC recommends retaining requirements to maintain inventories of samples containing biological select agents and toxins, while ensuring that BSAT institutions are not requested to characterize biological agents quantitatively.

Many responders objected to the detailed vial-by-vial inventory requirements of the SAR on the grounds that this type of inventory is not appropriate for replicating organisms. These responders argued that a microscopic amount of a sample can be imperceptibly removed from any select agent sample and used to grow an arbitrarily large, and undocumented, culture. They also argued that discrepancies between actual inventories and their corresponding databases are far more likely to result from bookkeeping errors than from the theft or diversion of actual samples. Therefore, these responders questioned the value of detailed inventories on the grounds that correlation of databases with physical samples can neither confirm that a diversion has taken place nor assure that it has not.

The FTAC agrees with this analysis. However, it also believes that institutions possessing BSAT are obligated to know and document what is stored in their laboratories and where those agents and toxins are located. It is therefore appropriate to require institutions to maintain inventories of their select agent stocks and be able to show not only that all their samples are documented, but that all entries in an inventory database correspond to physical samples. Maintaining and validating select agent inventories are essential elements of responsible conduct, even if they cannot be used to rule in or rule out a theft or diversion.

Correlation of database and physical stocks is therefore an indicator of quality management, and entities should practice accountability. The SAR do not require quantitative inventory controls for select biological agents, only for select toxins. The FTAC therefore recommends that accountability in the SAR be maintained at the level of identifiable physical items, such as vials or plates, and not extended to quantitative measurements of the size, volume, mass, or concentration of biological agents (other than as needed to describe them qualitatively). Currently, record keeping and inventory validation do not require accounting for and verifying biological agent concentrations or volumes. The FSAP should ensure that inventory validation through quantitative sample characterization (such as by thawing a frozen sample to measure its volume) is not occurring during inspections, except with toxins where appropriate. Quantitative sample characterization could otherwise needlessly degrade or destroy samples.

7. Consistency of Inspections: The FTAC recommends development of an approach to improve the consistency of the inspection process across inspectors, inspecting agencies, and inspected sites.

Respondents cited the loss of significant time, effort, and financial investment to reconcile inconsistent inspection results and inconsistent interpretation of regulations

among inspectors. Many larger laboratories and facilities undergo multiple inspections annually by various agencies. Inspectors from different Federal agencies, or inspectors from the same agency arriving at different times, often have differing standards and interpretations of the SAR, which lead the laboratory to engage in compliance actions that may not meet another inspector's compliance standards during future inspections. In addition, respondents outlined other factors that create inconsistency in inspections: a lack of pre-inspection communication by lead inspectors regarding changes to the scope and process of the inspection, as well as new regulatory interpretations when there is a change among case managers at regulatory institutions. Although there have been significant improvements over the past several years in coordinating inspections across agencies, stakeholders consistently identify this as a major issue. The FTAC recommends that the FSAP gather concrete examples of the inconsistencies and issues identified by stakeholders and develop an approach to improving the consistency of inspections and resolving these persistent issues, recognizing that solutions proposed in Recommendation 1 may help address these concerns.

8. Improve Customer Service in Communicating with Regulated Entities: The FTAC recommends improving communication before and after site inspections and improving the timeliness of inspection reports.

Respondents said that communication between inspectors and regulated institutions needs significant improvement. Many respondents believe the speed and method of communication would be greatly improved if paperwork and other written communication could be transmitted through a protected electronic mechanism rather than using paper and fax submissions. The FTAC strongly recommends that CDC and APHIS implement an electronic communication mechanism within one year of the release of this report to improve the efficiency and speed of communication.

Other examples of deficient communication include (1) delays in issuing inspection reports such that facilities cannot address compliance issues before subsequent inspections and (2) delays in receiving approval for new experiments, causing investigators to miss grant application deadlines. Moreover, while CDC requires responses from institutions within 30 days of inspection, the agency might take much longer to respond to laboratories on their proposed changes, amendments, and inspection reports, delaying research that cannot be done without approval. The FTAC strongly recommends inspection reports be communicated to registered facilities within 30 days of the inspection and that customer service performance metrics be established, monitored, and publicly reported.

9. Categorize Inspection Findings: The FTAC recommends developing a system to categorize findings on inspection reports.

Respondents noted that recorded violations received equal treatment, whether they were minor administrative errors or egregious safety or security violations. In addition, the lack of discrimination between a minor and a serious violation presents a communications challenge when a facility choses to share information regarding its regulatory compliance with the community or other members of the public.

The FTAC recommends categorizing observed SAR violations into one of three groups: administrative, important, or critical. Although more detailed definitions would have to be developed, critical violations would be those that have the potential to create a serious security or safety problem; important violations would be those having the potential to compromise the safety or security of the laboratory and staff, possibly in conjunction with other errors; and administrative violations might involve paperwork or documentation errors. The FTAC recommends the FSAP develop rigorous definitions for each category within 120 days of this report's release.

Finally, some stakeholders also suggested that, in addition to the focus on identified violations, facilities receive feedback on those aspects of regulatory compliance where they are doing well. The FTAC recognizes that this would be difficult to accommodate within a regulatory framework; other than attesting to regulatory compliance, inspectors are not in a position to opine on if, or by how much, the regulatory institutions exceed expectations.

10. Appeals Process: The FTAC recommends expanding the appeals process for institutions to adjudicate disputed findings in inspection reports.

Respondents expressed concern that there is no formal mechanism for engaging with the FSAP regarding disagreements, misunderstandings, or disputes with respect to inspection findings. The FTAC recommends that a timely and formal process be established for laboratories to resolve differences over inspection outcomes.

11. Peer Advisory Mechanism: The FTAC recommends creating an expert panel or Federal Advisory Committee to serve as an external group that could share best practices or make recommendations to the FSAP.

Respondents expressed a desire for greater peer-to-peer involvement with the FSAP. Respondents wished for a process by which they would be able to interact with the FSAP to provide subject-matter expertise on the SAR on a regular basis. To provide broader scientific and security viewpoints and advice, the FTAC recommends that HHS and USDA establish a framework of external scientific and security experts drawn from regulated communities, those having regulatory experience, and other relevant communities. This framework could be formed as a Network of Experts, as used by FDA, which provides opportunities for individual consultation. Alternatively, the framework could be a formal

Federal Advisory Committee, reporting to the FSAP, which provides consensus recommendations. Forming the latter would likely entail budgetary actions, but could be beneficial in building trust with regulated entities.

12. International Engagement: The FTAC recommends international engagement to explore harmonization of pathogen security standards and ensure understanding of the rationale for, and implementation of, the SAR-equivalent standards by collaborating foreign governments.

Respondents emphasized that rigorous pathogen security measures applied to select agents in the United States, if not complemented by the adoption of analogous measures internationally, would have only partial safety and security benefits and at the same time potentially harm U.S. research, since international competitors would not face an equivalent regulatory burden. One respondent also expressed concern that if the SAR were not adequately explained to foreign audiences, they could be misconstrued in ways that would be counterproductive to international dialogue on a range of issues, including access to, and sharing of, the benefits of research activities. The FTAC notes that the U.S. Government has been actively promoting the development of systems of biosecurity oversight both bilaterally and in appropriate multilateral forums for a number of years, and although the details vary, national oversight systems for biosafety or biosecurity are increasingly common among countries with significant life science research enterprises. Nevertheless, the FTAC agrees with the importance of such international engagement and recommends sustained and increased efforts by the Federal Government to both promote such oversight and to explore opportunities to harmonize regulatory approaches to the extent feasible.

13. Guidance for Customs Inspectors: The FTAC recommends providing better training and guidance for customs inspectors who process BSAT shipments.

Several respondents referred to incidents in which shipments of select agent materials had been delayed because customs officials were unfamiliar with the SAR, including cases where samples were degraded due to the delay and being stored at room temperature. Customs inspectors have also requested better connectivity to relevant sources of technical expertise—available at any time—for guidance on what to do with packages that arrive damaged and how to address associated exposure risks. Although the frequency of such events is unclear, the FTAC recommends that the Department of Homeland Security work with the FSAP to develop clear guidance and familiarization training for customs inspectors.

E. Issues for Further Analysis

The FTAC has identified several additional proposals for improving the SAR that could not be analyzed and assessed during FTAC's charter, including some issues that would require far-ranging change. The FTAC recommends continued analysis of these proposals to determine whether they would be advisable and, if so, to develop concrete approaches for implementing them. It is recognized that for some of the proposals, significant changes to the statute authorizing the SAR would be required.

A. Institutional Scope of Regulation: Consider whether to bring all bioscience institutions, or at least all those operating at or above Biosafety Level 3 or "high containment", under Federal biosafety regulation.

In the time available, the FTAC was not able to recommend one or the other of these proposed approaches or to develop an alternative. Instead, it recommends that a task force be charged with making proposals on whether and how the Federal Government should regulate biosafety of non-select agents, particularly those requiring containment at or above Biosafety Level 3. The FTAC does, however, caution against the inappropriate application of the SAR's security requirements to agents that pose primarily safety concerns.

Legislation initiating controls over the transfer of BSAT (the Antiterrorism and Effective Death Penalty Act of 1996; Public Law 104-132) and their possession, use, and transfer (the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Public Law 107-188) was enacted in the wake of security incidents involving hazardous pathogens; the original motivation for these laws was not to regulate safety. However, the current SAR serve both security and biosafety objectives. Specifically, the SAR require that registered individuals or entities "develop and implement a written biosafety plan that is commensurate with the risk of the select agent or toxin, given its intended use."[14] The regulations go on to specify a number of biosafety guidance documents that should be considered in the development of this plan. But these guidance documents, such as the CDC/National Institutes of Health publication "Biosafety in Microbiological and Biomedical Laboratories (BMBL)," are not written in the form of prescriptive regulations, and they do not themselves have the force and effect of law.

The FTAC received a wide range of views with respect to broadening the way in which biosafety should be regulated. Several respondents appreciated that in addition to its security rationale, the FSAP provides Federal oversight, inspection, and control of biosafety for work done with BSAT, and some argued that biosafety for all biological agents requiring high-containment or above facilities (e.g., Biosafety Level 3 or above) be similarly regulated. At present, agents such as multi-drug resistant *Mycobacterium tuberculosis*, Japanese encephalitis virus, St. Louis encephalitis virus, rabies virus, or

[14] See 42 USC 73.12(a), 7 USC 331.12(a), 9 USC 121.12(a)

Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) require the use of Biosafety Level 3 facilities, but they are not deemed to pose the security concerns that would warrant their designation as select agents.

Since the security requirements of the FSAP are unnecessary for these agents and would significantly impede research and other activities with them if applied, placing them under biosafety regulation would either require creating a biosafety-only regulatory regime, or it would require splitting the security requirements of the SAR from the safety requirements and generalizing the latter. These approaches likely would require statutory changes. They would also require defining "containment laboratory" or biosafety levels concretely enough to make clear which laboratories would be regulated, but generically enough to accommodate the wide range of objectives for which containment laboratories are constructed and the wide range of technical activities that are performed within them.

.

B. Possible Exemptions for Quality Assurance: Consider creating exemptions from certain security regulations for laboratories that retain certain select agents only for the purposes of positive control material availability and quality-assurance procedures.

The FTAC recommends that a future task force examine whether provisions can be made to ease the burden of SAR compliance for diagnostic, clinical, or food industry laboratories that work with BSAT without impairing the security benefits for controlling BSAT at other facilities.

Respondents from many clinical or diagnostic laboratories, or who worked in the food industry, reported that the SAR imposed undue burdens on those who, like themselves, retained select agents only for the purpose of validating their laboratory procedures, or for use as reference standards or positive controls to ensure that analytical tests were correctly identifying or characterizing the presence of select agents. They proposed that they not be burdened with the full panoply of SAR compliance, particularly with respect to the need for the FBI to conduct a Security Risk Assessment on each person with actual or potential access to BSAT and the need to keep detailed inventories.

The FTAC appreciates these concerns and recognizes that many organizations have robust hiring procedures to help ensure the honesty and integrity of the employees that they hire. But it also recognizes that the security value of controlling access to BSAT in any given facility has little to do with the purpose or the extent to which those agents are used in that facility. Therefore, the FTAC suggests that a task force, with appropriate input from the regulated and the security communities, examine the possibility of alternative approaches to achieving the overarching security goals for select agents in these types of dedicated-purpose laboratories. The alternative approaches would need to balance the risk

of misuse specific to this set of activities and institutions with the risk that if nothing is done, these laboratories may find it impossible to continue using BSAT for quality assurance.

C. Security Expenses: Examine mechanisms for funding security-related expenses for use of BSAT; determine if those mechanisms are adequate; and if not, propose options to ensure that funding is available for necessary security measures.

The FTAC recommends that the appropriate Departments and Agencies in the Federal government, as well as Office of Management and Budget (OMB) and OSTP, explore the costs associated with conducting work with Tier 1 BSAT as compared to other infectious agents and toxins requiring the same biocontainment levels; identify mechanisms for funding security-related expenses; determine if those mechanisms are adequate; and if not, propose options to ensure that funding is available for necessary security measures.

Many institutions registered to possess and use Tier 1 select agents noted that the costs of the security requirements associated with these agents are substantially higher than those corresponding to research with non-select agents, or with non-Tier 1 select agents. Funding agencies and funded institutions should work together to understand what the actual costs are, compared to work with other infectious agents and toxins at the same biocontainment levels, and whether current funding mechanisms, including the negotiated indirect expense reimbursement rates that federally funded research institutions are allowed to charge, are sufficient to cover these security expenses. Note that some institutions using BSAT, such as public health laboratories, may not be conducting federally funded research or collecting federal reimbursement for indirect expenses, and options that rely on federal research funding mechanisms would not address those institutions.

D. Consistent Disclosure Policies: Seek to ensure that institutions regulated under the SAR fall under consistent information-disclosure policies, to the extent that State and local laws and regulations pertaining to these institutions can be reconciled with Federal requirements.

The U.S. Government should explore ways to reconcile any contradictory Federal, State, and local regulations and policies, either by relaxing Federal protections or by enacting Federal statutes to extend to the State and local level the current protections against releasing certain security-relevant information under Federal Freedom of Information Act (5 USC § 552) requests.

Notwithstanding Recommendation 2 above, which promotes the disclosure of information relevant to the operation of laboratories regulated by the SAR, there will continue to be a need to withhold some security-related information concerning BSAT

research from public release. This need may extend to vulnerability analyses addressing the possible environmental release of certain organisms or the publication of Dual Use Research of Concern (i.e., research that has legitimate applications, but that generates materials or information that could be misused to cause harm), lest these vulnerability analyses become available to potential adversaries intent on exploiting those vulnerabilities.

The legislation establishing the FSAP required the program to protect certain SAR-related information from release under the Freedom of Information Act. However, BSAT laboratories operated by State universities or other State Governmental offices are subject to State open records or freedom of information acts, against which the Federal statutory language provides no protection. The FTAC recommends that this discrepancy be addressed to the extent possible, recognizing that the 10th Amendment to the U.S. Constitution restricts the Federal Government's ability to direct actions of State or local government.

E. Common Chemical, Biological, and Radiological Security Framework: Explore the feasibility of establishing a common interface for institutions—with respect to personnel vetting and personnel reliability—for people with access to chemical, biological, and radiological materials of security concern.

The FTAC recommends a Federal task force study the feasibility, cost, and benefit of integrating chemical, biological, and radiological personnel vetting, particularly for personnel suitability, to identify opportunities to make the vetting more thorough and efficient. If necessary, specific recommendations for changes in the relevant statutory and regulatory regimes should be developed.

Respondents pointed out that institutions that possess BSAT often also possess radioactive materials regulated by the Nuclear Regulatory Commission or chemical materials regulated by the Controlled Substances Act and other statutes or regulations. Although regulated in separate regimes, these materials can pose threats to public health and safety. Respondents recommended that there be an exploration of the potential for the regulatory regimes for these materials to be harmonized, recognizing that biological organisms naturally occur in the environment and replicate, as contrasted with nuclear and chemical materials.

The FTAC is supportive of the aspiration behind this recommendation, but recognizes that while the various regulatory regimes involved share some common elements, the various requirements are designed to reflect the unique nature of each material/agent. For example, nuclear-related vetting of personnel is concerned with proliferation of knowledge to non-nuclear regimes, whereas international collaboration in BSAT research is encouraged. As a result, the analytic approach to vet and register people who use or possess these materials, as well as the nature of the hazard they pose, the means to protect public

safety, and the executive branch departments or agencies with regulatory authority, are quite different. It is worth exploring whether there are areas for the institutions to better communicate with the U.S. Government to more seamlessly and efficiently vet individuals. Note, however, that any changes may require amendment not only of the statutes and regulations governing the FSAP, but the other statutory and regulatory regimes as well. The FTAC believes that further study is required to understand whether it would be feasible and desirable to merge aspects of the personnel-vetting process governed by uniquely tailored CBRN (chemical, biological, radiological, and nuclear) regulatory regimes. Therefore, a Federal task force should be charged to study this issue further and develop specific recommendations.

F. Risk-based Approach: Explore the feasibility of adopting a "risk-based" approach to managing the safety and security oversight of biological agents and toxins.

The FTAC recommends that the National Science and Technology Council charter a working group to examine the feasibility of developing a more holistic risk-based approach to biosafety and biosecurity. The FTAC notes that the SAR only address agents and toxins that are determined to be BSAT. Second, the SAR only address those security risks that result from physical access to a listed pathogen. Security risks from the information generated while working with pathogens (whether listed or not), or from physical access to unlisted organisms that have been genetically modified to confer pathogenic properties, cannot be accommodated through the SAR in their current form. Some, but not all, of these risks are currently addressed through other instruments, including Federal policies concerning the funding of "dual-use research of concern" (DURC) and an ongoing review of Federal policy in relation to so-called gain-of-function research; however, these policies lack full legal force and effect and are limited in scope.

Given that emerging infectious diseases and the ability to manipulate virulence or toxicity factors at the molecular level present potential risks and challenges, a risk-management tool or algorithm may provide a more appropriate means than a list-based approach to managing risks to laboratory workers and the environment. At the same time, developing a purely risk-based approach that can be applied for security purposes (e.g., to require suitability vetting of personnel) may prove challenging.

In 1997, the SAR framed a list of dangerous pathogens to control the distribution and access to agents based on the following criteria, as stated in the Antiterrorism and Effective Death Penalty Act of 1996:

> the effect on human health of exposure to the agent; the degree of contagiousness of the agent and the methods by which the agent is transferred to humans; the availability and effectiveness of immunizations

> to prevent and treatments for any illness resulting from infection by the agent; and any other criteria that the Secretary considers appropriate.[15]

The FTAC recognizes that the select agent list is not static. Although there is an established process for its biennial review and modification, it is still a list. With the creation of the Tier 1 designation (Executive Order 13546), several registered entities decided to forego working with the Tier 1 BSAT to avoid increased compliance costs. In other cases, those entities that decided to continue working with Tier 1 BSAT used this change in the SAR as an opportunity to segregate this work from other activities that would not need to meet Tier 1 requirements.

Throughout the multiple Federal and nongovernmental reviews and public comments in the past, including this current effort, it is clear that there is tension and discomfort with the select agent list. On the one hand, the list allows the imposition of regulatory requirements. On the other hand, other pathogens of concern to public health do not meet the criteria for consideration as a select agent and are therefore would be inappropriate to add to this list. Moreover, new technologies and DNA manipulation techniques may not be addressable in the context of a list-based approach at all.

Stakeholders are part of a community that wants to employ the best practices available to enhance laboratory safety and security, and their inputs show that the field is at a significant enough crossroads to consider a more robust risk-based management approach with an eye to both a list (requiring safety and security measures to be applied to certain organisms) and a method of assessing risk management and mitigation. This Issue differs from Issue A (above), which would extend the safety aspects of the current regulatory regime to a broader set of pathogens. The analysis performed under this Issue would address a new regime that replaces many of the specified safety and security requirements with a more integrated, risk-based approach that is better able to address the full spectrum of biological risks, particularly those resulting from the evolution of biotechnology and research techniques.

G. Shipping Regulations: Review domestic and international shipping regulations and requirements, as well as related guidance, with a view to simplifying and clarifying, and to facilitating compliance by other countries.

A number of respondents raised concerns with Federal shipping regulations for BSAT. Some noted that compliance with these regulations is costly, but others commented that relatively few shipping companies were willing to handle select agents and toxins and that shippers and customs officials did not in all cases appear to understand the regulations. One respondent noted that the complexity of regulations posed particular challenges for other countries and was harming scientific collaboration. The FTAC recommends that the

[15] See Pub. L. No. 104-132, 110 Stat. 1284.

Department of Transportation, in consultation with FSAP, review the relevant regulations and the availability of clear, readily accessible guidance materials to facilitate communication and compliance.

Appendix A
Summary of Comments from Listening Sessions

This appendix includes the summary notes from two non-attribution listening sessions of stakeholders convened by the Office of the Science and Technology Policy and the FTAC to share individual views and comments on the effect of the SAR on science, technology, and national security. The first meeting took place on February 17, 2015; the second meeting on March 20, 2015. This appendix highlights representative comments and perspectives expressed during the sessions. Table A-1 lists the number of stakeholders, by affiliation category, in attendance.

A-1. Listening Session Attendees by Affiliation Category

Affiliation Category	# of Attendees
Accounting and Law	2
Other	4
Professional Societies	3
Public Policy Institutions	6
Research Institutions	2
State Public Health Laboratory	5
Universities	11
U.S. Government (Non-FTAC)	22
Grand Total	**55**

Stakeholder Input from the Meeting of February 17, 2015

Comments on the Overarching SAR Approach (system of reporting, safety, and security rules tied to a specific list of pathogens and toxins)

- The current list of select agents is sound and could even be augmented to include MERS-CoV. Some consideration should be given to address synthetic and gain-of-function organisms in a mechanism similar to the current SAR approach.
- SAR have improved laboratory safety and security across the country.
- There should be equal emphasis on biosafety and biosecurity. Inspection is too focused on checklist approach. Inspectors must assess overall safety and security in a local context.

Costs and Benefits of the Current SAR Process (inspections, administrative processes, regulatory transparency and communication)

- There have been significant delays in paperwork processing, including receiving inspection reports after an inspection (6+ months) and paperwork requests for non-substantive amendments (4+ months), and closeout reports after inspection report correspondence. These delays have impeded the ability of scientists to conduct research.
- Inventory stocks of potential scientific value have been destroyed because regulatory verification standards proved to be too challenging.
- Following the establishment of the Tier 1 list of select agents and associated regulations, some institutions decided to abandon research with Tier 1 select agents because the financial costs associated with compliance were too high.
- The financial costs of physical security regulations and personnel suitability regulations, particularly around Tier 1 agents, are placing substantial burdens on many institutions.
- A majority of participants reported the current supply of investigators and trainees is shrinking because of burdensome regulation. Others, however, believed that might be the result of a natural contraction of personnel working on select agent research after a 15-year period of overexpansion.
- Administrative requirements have caused delays in the time needed to transfer a select agent. In some instances these delays have exceeded the acceptable time requirements, resulting in the destruction of cultures and the loss of valuable research material.
- Participants cited inconsistent interpretation of vague regulatory language regarding inventory management requirements and physical security specifications.
- Budgetary constraints associated with SAR at public health laboratories result in scarce resources that are inadequate to address laboratory acquired infections and deliberate release events.
- Several manufacturers have decided to stop producing veterinary vaccines or diagnostics due to a combination of rising SAR compliance costs and small profit margins for those products. For example, it costs twice as much to develop a vaccine for EEE as for WEE.
- The cost of Tier 1 SAR has led many Food Safety Inspection Service laboratories to cease their work with Tier 1 agents, possibly weakening a public health emergency response involving the food supply.

- Inconsistent regulations and standards for biohazard waste management discourage hospitals from taking patients infected with select agents, hindering the public health response.

Recommendations to Improve SAR Process

- Suggestions for redesigning the inspection process included reformatting the inspection reports such that "observations" could be categorized into distinct tiers of security and safety concern. Currently, the observed violations carry the same weight whether they are typographical errors in a report or egregious security violations.
- Many participants reported the need to improve communication between regulators and regulated community. Recommendations include creating an active and systematic feedback mechanism to allow regulated community to provide constructive comments and cite-specific risk assessments.
- A need exists for greater flexibility to incorporate agents on the select agent list.
- There is a need for an online system to facilitate the amendment process, using electronic submission technology rather than fax. The forms themselves need to be more streamlined.
- Current guidance on personnel security and suitability expectations is insufficient, and more guidance is requested.
- Participants suggested lengthening the select agent transfer time period to account for administrative delays.
- Excluding physical security features, there should be more disclosure of information regarding select agents and stronger engagement with the public. Suggestions include creating a website to highlight lessons learned about laboratory incidents and provide fact-based information for the public.
- Public health laboratories are underfunded, work with very limited amounts of select agents, and do limited types of manipulations. One suggested approach is to stratify Tier 1 agents based on type of agent to provide a tailored risk-management approach.
- Clear SAR are needed to guide the interface of select agent diagnostic laboratories with medical facilities that treat select agent patients.

Gaps in the Overarching SAR Approach or Process

- Currently, it is difficult to conduct international select agent research collaborations. Many international laboratories are not as well funded as entities

in the United States, and it remains unclear how to SAR will affect the global engagement of U.S. entities that have international collaborators.

- Gain-of-function experiments and synthetic organisms that are created to be nearly identical to select agents represent a daunting challenge that may require an approach beyond the current SAR approach.
- There is a dearth of best practices and benchmarking data on the financial costs associated with optimal implementation of regulations associated with various select agent research activities.
- Inspectors have difficulty putting SAR in the context of activities conducted in a state public health laboratory.

Comments on Additional Approaches

- As suggested by the Defense Science Board and the National Science Advisory Board for Biosecurity, SAR are not sufficient by themselves. An improved leadership role from the Federal Government and a stronger culture of personal responsibility are also important components of biosecurity and biosafety.

Stakeholder Input from the Meeting of March 20, 2015

Comments on the Overarching SAR Approach (system of reporting, safety, and security rules tied to a specific list of pathogens and toxins)

- The SAR is the only regulation that addresses laboratory safety and requires inspections, which provide an extra impetus for laboratory personnel to be more diligent in working with select agents.
- While some participants favored a list-centered approach to classifying select agents, many suggested revising groupings on the select agent list to discern between agents that pose biosecurity risks and food pathogens that affect food safety. There was interest in amending the list to include additional agents (such as Ebola and meningitis), while removing agents used in food challenge studies.
- Some participants suggested a move away from an agent-centered approach to general approaches and systems for improving safety and security with all pathogens, not just select agents.

Costs and Benefits of the Current SAR Process (inspections, administrative processes, regulatory transparency and communication)

- Participants indicated a general "love-hate relationship" with respect to the SAR in that it provides many benefits to the laboratories, but comes at a cost in terms of time and money.
- SAR allows laboratories to have better understanding of protocols in processing of human samples, provides guidance in whether a sample needs to be inactivated, helps ensure there are no unauthorized releases from laboratories, ensures decontamination of instruments, etc.
- While there are areas for improvement, inspections have been positive, have provided good models to deal with inventory of all organisms and agents, and have provided a system of security checks so that more focus is on the science.
- Implementing SAR requires much time and money, especially with regard to time spent in inventory controls and cost of hiring additional staff to handle paperwork and adhere to regulations.
- The high cost of maintaining Tier 1 facilities has resulted in numerous institutions opting out of Tier 1 research. Food safety laboratories in particular are now using surrogate agents, which pose a risk to public health.
- In general, researchers have begun to move away from select agent research due to burden of adhering to SAR.
- Personnel approval is an issue, as there is a long timeline for approval, and the limited number of SAR-approved staff can cause delays when one or more are unable to work. In addition, approved personnel should have the necessary scientific background to contribute to the science.
- Personnel suitability and background checks provide peace of mind for bigger laboratories and allow research organizations to focus on science.

Recommendations to Improve SAR Process

- Additional guidance is needed in determining personnel suitability. Suggestions included sharing personnel reliability across institutions and looking at the Department of Defense's personnel reliability program, which includes certification of officials, and involving supervisors and occupational health doctors.
- Respondents recommended changing the inspections process to foster mutual respect and greater collaboration between institutions and regulators. Inspectors could do more outreach to the community by giving talks, utilizing individuals from other institutions as part of the inspection team, and providing positive

feedback (in addition to noting areas for improvement). One recommendation was to look at ALAC accreditation process.

- Communication between institutions and inspectors should also be improved, especially in terms of receiving more timely feedback, amendments, and inspection reports from regulators.
- Trust is important in personnel reliability program. One suggestion was to add a code of conduct to regulations.
- In the event of an exposure, participants said that there is no clear guidance from the CDC on how to respond.
- To increase efficiency in implementation of SAR, respondents suggested a move toward having paperwork associated with select agents in an electronic or online format.
- Participants suggested that the focus of inspections should be on larger errors that post biosecurity risks, moving the focus away from small details that are singular person errors (vs. large, systemic errors). In addition, there are problems in interpretation of regulation by different inspectors.
- For larger institutions that have appropriate safety and security measures in place, special consideration should be given to making decisions on restricted experiments while keeping CDC informed, because approval processes often do not allow for short timelines.
- For institutions that are already registered as select agent institutions, one recommendation was to simplify the process for registration of additional agents if the institution is already registered for the same or lesser level to avoid going through entire process again.
- Many laboratories also work with radioactive materials and have security measures in place. One recommendation was to streamline guidelines for select agents and radioactive materials.

Gaps in the Overarching SAR Approach or Process

- In addition to providing laboratories feedback on improvements, regulators should also provide feedback on things that are done well, and these could be shared as best practices across institutions. There is interest in creating a centralized database of best practices, specifically creating a database for inactivation protocols.

- A suggestion was made to include minimum standards in the SAR, especially for distinguishing Tier 1 from non-Tier 1 security standards, video surveillance of storage, archiving, information security, and psychological monitoring.
- Participants emphasized the importance of conducting risk assessments, with one recommendation for principal investigators to submit risk assessments at the start of each new project.
- There is a need to for studies on the impact of use of select agents on instrumentation, and an evaluation process needs to be developed for safety and security when using mass spectrometry instruments.
- To build a better culture of safety at all staff levels, training programs and continuing education should be offered to all staff.
- The Global Threat Reduction Initiative (GTRI) provides a model for improvements to SAR implementation and uptake in institutions. The GTRI provides recommendations to laboratories, incentivizes them to make improvements, and provides training.

Comments on Additional Approaches

- To improve consistency and communication of the SAR, a recommendation was made to change the management and oversight of the SAR from Federal to an independent agency that neither funds nor conducts select agent research.
- One challenge in applying regulations is having different settings—industry, university, government, all of which have different cultures. How regulations are taken up and implemented is affected by these cultures.
- The culture of biosafety at institutions should be encouraged by top management to all staff levels so that there is less emphasis on regulations and more on individuals promoting safety and security.
- There is an issue of unbalanced perspectives as SAR laboratory personnel think SAR is an undue burden but the community thinks not enough is being done. Improvements in inspections and community outreach can improve the balance.