Fast Track Action Committee Report:

Recommendations on the Select Agent Regulations Based on Broad Stakeholder Engagement

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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.

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[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.

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[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

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[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.

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[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.

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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.