towards mitigating the risk of an insider threat to warrant the additional, significant burden on research institutions; and 3) a PRP is likely to have unintended and detrimental consequences for the scientific enterprise that in the future could result in more harm to public health and safety and to national security than an insider threat poses.

2. **The current SRA process should be strengthened.** The SRA is a valuable federal-level check of an individual's possible criminal history and potential terrorist ties. To further strengthen the SRA, the federal government should continue to identify potential weaknesses and gaps in the information-gathering process, and adjust the procedures as necessary. However, the SRA should remain a timely process so as not to impede the recruitment of researchers, including foreign researchers. In its full report, the NSABB has noted several examples of how the SRA process could be strengthened.

3. **The culture of responsibility and accountability should be enhanced at institutions that conduct select agent research.** Though persuasive evidence is lacking that PRP assessment instruments can effectively identify individuals who pose an insider threat, enhancing the culture of responsibility and accountability among individuals with access to select agents and toxins is a way to strengthen personnel reliability. This can be accomplished without any significant expenditure of resources or disruptions of research, and was noted by many whom the NSABB consulted as being the best defense against the insider threat.

   In this context, the NSABB identified a goal that every institution that conducts research on select agents should strive toward, as well as a set of Guiding Principles for the responsible conduct of research on select agents and toxins that underpin the issue of personnel reliability. In addition, the NSABB identifies several specific practices and approaches for enhancing the culture of reliability and accountability at the institutional level.

4. **Professional societies should continue to encourage an ongoing dialogue about personnel reliability to maintain vigilance about biosecurity issues throughout the research community and to foster community-based solutions.** Many professional societies have done a commendable job engaging their respective communities both in the U.S. and internationally about Dual Use Research of Concern (DURC).[8] These societies should now strengthen their conversations about maintaining personnel reliability as they promote a culture of research responsibility and vigilance about DURC and other biosecurity issues. Outreach and education efforts will be essential to enhancing the culture of research responsibility outlined above as this culture will be fostered by individuals who are knowledgeable about the insider threat, trained in appropriate security measures, and have a clear understanding of their role within a select

[8] National Science Advisory Board for Biosecurity, *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information* (Washington, DC: 2007). Dual use research of concern is described on page 17 of this report as "[r]esearch that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agriculture, plants, animals, the environment, or materiel." The NSABB report can be accessed at oba.od.nih.gov/biosecurity/biosecurity_documents.html (accessed May 5, 2009).

agent research facility. Professional societies are well-positioned to undertake these outreach and education efforts and to equip researchers with the tools required to strengthen vigilance about biosecurity at the local level.

5. **The *List of Select Agents and Toxins*[9] should be reduced or stratified.** The currently designated select agents differ significantly in degree of pathogenicity and ability to be utilized as an agent of bioterrorism. Consequently, the risk that they might pose to public, animal and plant health and safety varies significantly depending on the agent, and yet the same stringent controls apply across the board, making it unnecessarily very difficult to conduct vital research on these important biological organisms by hindering the ability of less pathogenic select agents to be used for legitimate research purposes.

   The select agent list is reviewed every two years in recognition of the emergence of new potential agents. These compulsory reviews should continue with greater consideration for removing agents that research and management show to be of lower risk. The NSABB recognizes that the decision to remove agents from the list should not be taken lightly and will require much consideration from the scientific and public policy-making communities. Although certain agents may be removed from the *List of Select Agents*, research using these strains is and would still be conducted at the appropriate biosafety level with all the specified safety and appropriate security precautions. While there is a process to remove attenuated (or weakened) strains of select agents that pose little or no risk to public health and national security from the list, the process is considered unduly complex, burdensome, time-consuming and inhibitory to research. The process thus needs reconsideration.

[9] The current *List of Select Agents and Toxins* can be found at www.selectagents.gov/resources/List of Select Agents and Toxins_111708.pdf (accessed May 8, 2009).

Introduction:

Purpose of this report. The National Science Advisory Board for Biosecurity (NSABB) was charged with recommending to the United States Government (USG) strategies for enhancing personnel reliability among individuals with access to biological select agents and toxins.[10] The challenge is to develop policies aimed at mitigating the risk of misuse of select agents by individuals who have access to them as part of their jobs, education, or training, the so-called "insider threat," and appropriately address biosecurity concerns without unduly hindering the pace of life sciences research. This report is intended to provide guidance to the USG as it designs such policies, and sets forth the NSABB's recommendations for enhancing personnel reliability by building on the existing Select Agent Program and calling for renewed sense of responsibility and accountability among researchers at the institutional level.

The critical role of select agent research. Protecting public health and safety and maintaining national security depend in large part on a robust and agile life sciences research enterprise that utilizes a diverse workforce spanning government, private, and academic sectors. Some of this research focuses on certain highly pathogenic organisms and toxins designated as "biological select agents." Research on these agents, and the mechanisms by which they cause disease or harm, underpins our ability to successfully combat infectious diseases affecting humans, animals, and plants, and is essential to the development of new and improved diagnostics, treatments, and preventative measures for a variety of infectious diseases, including the development of vaccines, therapeutic antibodies, antimicrobial treatments, and strategies aimed at augmenting the human immune response to more effectively target pathogens. Historically, research on pathogens or toxins that are now designated select agents, such as the variola virus, has resulted in vaccines and/or therapies that have greatly reduced the rates of human morbidity and mortality across the globe and, in turn, significantly lengthened the human lifespan. Research on other select agents shows promise of providing insights into emerging infectious diseases as well as other non-infectious diseases. Such research conducted on plant and animal pathogens has greatly contributed to the development of a safe and nutritious food supply that is readily available at a fairly low cost. A thriving select agent research enterprise broadly supports public health and safety, agricultural and commercial development, and economic competitiveness, as well as national security.

Such research also enables the development of effective countermeasures against bioterrorism threats because an in-depth understanding of biological select agents is essential to the development of new and improved detection and diagnostic technologies, antimicrobial and antitoxin treatments, and preventative measures, all of which will greatly enhance our capabilities not only to respond to acts of bioterrorism and to disease outbreaks but to develop

---

[10] Select agents are biological agents and toxins that have the potential to pose a severe threat to public, animal, or plant health, or to animal or plant products, and whose possession, use, and transfer are regulated by the Select Agent Rules (7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73). The current *List of Select Agents and Toxins* can be found at www.selectagents.gov/resources/List of Select Agents and Toxins_111708.pdf (accessed May 8, 2009).

beneficent uses. For example, anthrax lethal toxin has been shown to inhibit tumor angiogenesis and may have broad implications as an anti-tumor agent.[11]

The insider threat. In 2001, spores of *Bacillus anthracis* were sent to victims via the U.S. Postal Service, resulting in 22 infections, five deaths, extensive social disruption, and enormous costs for the emergency response, remediation, and subsequent investigation. The well-publicized FBI investigation that followed, which focused on U.S. scientists,[12] has resulted in renewed scrutiny of laboratory security. In turn, these heightened concerns surrounding the potential misuse of dangerous pathogens within research settings has resulted in calls to reexamine, and potentially enhance, the laboratory security measures aimed at ensuring personnel reliability among individuals with access to biological select agents and toxins.

The "insider threat" generally refers to the misuse of these pathogens by an individual who has access to them as part of his or her job. The scenarios that illustrate the insider threat are numerous, but they can generally be described as involving the theft, misuse, or diversion of a select agent by an individual who had been approved to have access to them. Some examples of the "insider" include an individual with malevolent intent who infiltrates a research facility under the guise of a legitimate researcher, only to steal, release or divert select agents, or an individual with access to select agents who is coerced into providing access or expertise to unauthorized individuals with malevolent intent.

Controls on access to select agents were significantly strengthened after the anthrax mailing incident.[13] Following the terrorist attacks of 2001 and the subsequent anthrax mailings, the USG substantially expanded the scope of the select agent regulations and added measures aimed at ensuring personnel reliability. Prior to 2001, the Select Agent Regulations were largely focused on shipping, requiring individuals and facilities that ship or receive select agents and toxins to register with, and report each transfer to, the Centers for Disease Control and Prevention (CDC) or the United States Department of Agriculture (USDA). The current Select Agent Rules[14] were expanded by the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*[15] (Bioterrorism Response Act) to require that all entities that possess or use (in addition to transport) select agents must register with the CDC or USDA.

---

11. Randall W. Alfano et al., "Potent inhibition of tumor angiogenesis by the matrix metalloproteinase-activated anthrax lethal toxin," *Cell Cycle* 7, no. 6 (2008): 745-49, www.landesbioscience.com/journals/cc/article/5627/ (accessed May 8, 2009).

12. In 2008 the Department of Justice announced its intention to seek a grand jury indictment against a U.S. scientist working in a federal research facility. These charges were not filed as the scientist took his own life. See DOJ Press Release, "Transcript of Amerithrax Investigation Press Conference," August 6, 2008, www.usdoj.gov/opa/pr/2008/August/08-opa-697.html (accessed April 30, 2009). To date, no further details regarding the anthrax mailings investigation have been made public and the NSABB was not briefed on the personnel reliability aspects of the investigation.

13. Spores of *Bacillus anthracis*, the pathogen that causes the disease known as anthrax, were sent through the mail in 2001. The NSABB notes that the colloquial expression "anthrax mailing" is imprecise as anthrax, the disease, was not mailed; however, this phrase is commonly used to refer to the mailing of these spores.

14. 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73.

15. *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*, Public Law 107-188, 107th Congress, 2nd Sess. (June 12, 2002), frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_cong_public_laws&docid=f:publ188.107.pdf (accessed May 8, 2009).

Both the Bioterrorism Response Act and the 2001 USA PATRIOT Act[16] address the concept of personnel reliability by declaring that certain types of individuals are prohibited from having access to select agents. Generally, a restricted or prohibited person is an individual who has committed a felony or been convicted of using illegal drugs, has engaged in terrorist activities, has a history of mental illness, or is a citizen from a country designated as a state-sponsor of terrorism. The specific restricted and prohibited categories are as follows:

Restricted and Prohibited Categories

A restricted person under the USA PATRIOT Act (18 U.S.C. 175b):

- is under indictment for a crime punishable by imprisonment for a term exceeding 1 year;
- has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year;
- is a fugitive from justice;
- is an unlawful user of any controlled substance as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802);
- is an alien illegally or unlawfully in the United States;
- has been adjudicated as a mental defective or committed to any mental institution;
- is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country that has repeatedly provided support for acts of international terrorism; or
- has been discharged from the Armed Services of the United States under dishonorable conditions.

A prohibited category under the Bioterrorism Response Act includes an individual reasonably suspected by any federal law-enforcement or intelligence agency of:

- Committing a crime specified in 18 U.S.C. 2332b(g)(5);
- Having a knowing involvement with an organization that engages in domestic or international terrorism as defined in 18 U.S.C. 2331 or with any other organization that engages in intentional crimes of violence; or
- Being an agent of a foreign power as defined in 50 U.S.C. 1801.

Under the current Select Agent Rules implemented by the U.S. Department of Health and Human Services (HHS)/CDC and USDA/APHIS (Animal and Plant Health Inspection Service), an individual requiring unescorted access to select agents as part of his or her job must have a Security Risk Assessment (SRA) by which his or her potential status as a restricted or prohibited person is evaluated. A favorable SRA is required for access to select agents. An individual must provide fingerprints and disclose aspects of possible criminal history, use of illicit drugs, mental-health history, and whether dishonorably discharged from the U.S. Armed Services.[17] Additional information is collected from naturalized citizens and permanent residents regarding immigration status and country of birth. Federal databases are then utilized to examine an individual's possible criminal background, potential terrorist ties, and immigration status (see databases in Appendix B). Additional investigation is conducted if necessary.

An individual granted access to select agents must undergo a new SRA every five years. Responsible Officials (ROs) and Alternate Responsible Officials (AROs) who oversee select

---

[16] *Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001*, Public Law 107-56, 107th Cong., 2nd Sess. (October 26, 2001) frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_cong_public_laws&docid=f:publ056.107.pdf (accessed May 8, 2009).

[17] Information is collected on the FBI form *Federal Bureau of Investigation Bioterrorism Preparedness Act: Entity/Individual Information*, also known as FD-961, available at www.fbi.gov/terrorinfo/bioterrorfd961.htm (accessed May 8, 2009).

agent research programs must obtain a favorable SRA each time the certificate of select agent registration is renewed. In addition, the FBI is automatically notified when an individual with a favorable SRA is arrested and fingerprinted or checked against criminal databases for whatever reason. The FBI also monitors individuals with favorable SRAs for criminal activity or terrorist ties by periodically cross-checking their names and fingerprints against federal databases. Access to select agents can be denied, limited, or revoked at any time by the institutional RO or ARO, the CDC, or the USDA if deemed appropriate. These decisions can be appealed.

The current Select Agent Rules also describe security, inventory, and personnel training requirements. In addition, there are civil and criminal penalties for non-compliance with the Select Agent Rules. Compliance with these regulations is critical as institutions and individual scientists engaged in select agent research have much at stake, including the safety of laboratory personnel, the safety of the public and the environment, and the public's confidence and trust in their ability to conduct such work safely and responsibly.

A focus on "biosurety" and personnel reliability. Historically, the concept of personnel reliability in research settings has been addressed as a constituent of larger surety programs. Surety programs were first implemented to prevent unauthorized access to chemical and nuclear weapons-related agents, and typically consist of four major components: (1) physical security, (2) safety, (3) personnel reliability, and (4) agent/material accountability.[18, 19, 20] "Physical security" describes both the structures and the individuals that secure and restrict access to sensitive materials. "Safety" encompasses the standards, practices, specialized equipment, and laboratory design features that help to ensure the safe handling of such agents, and protect the health of research personnel, the public, and the environment. "Personnel reliability" measures aim to ensure that individuals granted access to sensitive materials are trustworthy, responsible, and stable, and can competently perform their duties. "Agent accountability" involves procedures for maintaining accurate inventories and transfer records.

"Biosurety" is a term coined to describe the application of surety principles to research involving biological agents.[21] Although not labeled as such, some aspects of biosurety are currently addressed in life sciences research in the form of guidelines, manuals and best practices. For example, the CDC-NIH (National Institutes of Health) manual *Biosafety in Microbiological and Biomedical Laboratories* and the *NIH Guidelines for Research Involving Recombinant DNA Molecules* describe biosafety practices and procedures for work with pathogens and recombinant

---

18. Gretchen L. Demmin, "Biosurety" in *Medical Aspects of Biological Warfare*, ed. Martha K. Lenhart, 543–58 (Washington, DC: Defense Dept., Army, Office of the Surgeon General, Borden Institute, 2007).

19. Kathleen Carr et al, "Implementation of Biosurety Systems in a Department of Defense Medical Research Laboratory," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science*, 2, no. 1 (2004): 7–16, www.liebertonline.com/doi/abs/10.1089/153871304322964291 (accessed May 8, 2009).

20. Ross H. Pastel et al, "Clinical Laboratories, the Select Agent Program, and Biological Surety (Biosurety)," *Clinics in Laboratory Medicine*, 26 (2006): 299–312, www.sciencedirect.com/science/article/B75HR-4K991CB-5/2/17d59bd962ece152a61c4fc391c231b5 (accessed May 8, 2009).

21. The term "biosurety" stems from a historically weapons-related concept of surety that also encompasses the concept of quality assurance for weapons delivery. As such, "biosurety" is a misnomer in the life sciences context as, in accordance with the Biological Weapons Convention, the U.S. does not develop biological weapons. Accordingly, select agent research is not conducted to develop bio-weapons or with the intent of enhancing offensive capabilities. This report minimizes the use of the term "biosurety" to avoid the implication that such programs are weapons-related and focuses instead on personnel reliability.