

Responsible Research with Biological Select Agents and Toxins

The 2001 anthrax letter attacks prompted the creation of new regulations aimed at increasing security at laboratories conducting research with dangerous pathogens. This report evaluates current practices and recommends a set of principles and policies to help ensure that the demands of security are met while allowing vital research to continue and grow.

The effort to understand and combat infectious diseases has, over the centuries, produced many key advances in science and medicine—including the development of vaccines, drugs, and other treatments. A subset of this research is conducted with agents that, like anthrax, not only pose a severe threat to the health of humans, plants, and animals but can also be used for ill-intended purposes. Such agents have become known as biological select agents and toxins.



Photo by James Gathany, courtesy CDC

Research with biological select agents and toxins is subject to special regulations and requirements under the Select Agent Program, which is overseen by the U.S. Centers for Disease Control and Prevention (CDC) and the Animal and Plant Health Inspection Service (APHIS). Currently almost 400 institutions are registered with the Select Agent Program and approximately 15,300 individuals are cleared to have access to such agents.

Since the FBI announced its conclusion in 2008 that a researcher at the U.S. Army Medical Research Institute for Infectious

Diseases was responsible for the October 2001 anthrax letter attacks, concerns have grown as to whether regulations are adequate. This study was undertaken to evaluate both the physical security of facilities working with these materials and personnel reliability measures for those with access to biological select agents and toxins. The report offers a set of guiding principles and recommended changes to current practices that will help enhance the management of the Select Agent Program, focus attention

where it is most needed, and foster a culture of trust and responsibility that can satisfy both the demands of security and the ability of labs to conduct vital research.

The List of Select Agents and Toxins

The Select Agent Program and regulations govern research using materials on a list of just over 80 agents and toxins. The report concludes that the present one-size-fits-all list does not appropriately address the range of risks and vulnerabilities. Moreover, the number of items on the list dilutes attention that would be better

Guiding Principles

1. Research on biological select agents and toxins is essential to the national interest.
2. Research with biological select agents and toxins introduces potential security and safety concerns.
3. The Select Agent Program should focus on those biological agents and toxins that might be used as biothreat agents.
4. Policies and practices for work with biological select agents and toxins should promote both science and security.
5. Not all laboratories and not all agents are the same.
6. Misuse of biological materials is taboo in every scientific community.

focused on those evoking the greatest degree of concern and may, in fact, make the nation less secure. **The list of select agents and toxins should be stratified according to the agents' potential uses as biothreat agents, with regulatory requirements and procedures calibrated against this stratification.**

Personnel Reliability

Screening

Personnel screening seeks to identify individuals who may pose a potential security risk as early as possible, ideally prior to hiring. The proportion of job candidates who represent true security risks is unknown, but is likely to be very small. Efforts at screening for such individuals or behaviors struggle with dueling concerns. On the one hand, screening that is too relaxed may give access to the wrong people, but on the other hand, screening too strictly may exclude innocent individuals.

The current screening process involves an FBI check for a set of disqualifying behaviors or activities that automatically and permanently deny an individual access. The search relies on more than 20 federal criminal, immigration, and terrorist databases routinely used in security or suitability

screening for other federal agencies and, in some cases, the private sector.

After reviewing other approaches to federal personnel security and suitability screening, the report concludes that the current background checks conducted by the Select Agent Program are appropriate and consistent with U.S. government practices in determining the eligibility of individuals to handle sensitive information and materials. **Although the report recommends that the current screening be maintained, the appeal process should be expanded beyond a simple check for factual errors to include an opportunity to consider the circumstances surrounding otherwise disqualifying factors.**

With regard to other forms of testing, such as polygraphs, personality assessment tools, and integrity tests to assess potential counterproductive behaviors, the report concludes that there is no “silver bullet,” that is, no single assessment tool that can offer the prospect of effectively screening out every potential terrorist. Although such assessments might be used in screening for other reasons, they would not aid efforts to screen laboratory personnel for security risks.

Monitoring and Management

Once an individual is cleared by the FBI, that certification remains in effect for five years, with continued monitoring using selected databases and automatic notices in some instances, such as when an individual is arrested and fingerprinted. But this process cannot be expected to address all significant issues or personal changes that could occur in an individual's life during the five-year period of certification, including those that could potentially render him or her a security risk. Efforts to ensure personnel reliability will have to come from those laboratories where select agent research is conducted and specifically from increased engagement by managers and staff.

Encouraging results from research on insider threats suggest that cases in which an individual's action is genuinely spontaneous are rare. Most people follow a psychological path from idea to action and give signals along the way—including those who try to conceal their intentions. While no system can guarantee success in preventing an

illegal act, the warning signs occur often enough that it is reasonable to believe that active, sustained monitoring and management could detect many of them and provide the basis for prevention of dangerous behavior.

To support active monitoring and management, laboratory leadership and the Select Agent Program should encourage and support the implementation of programs and practices aimed at fostering a culture of trust and responsibility.

Consideration should be given to introducing personnel monitoring issues and educating personnel on the warning signs of insider threats during required training and safety inspections. More broadly, those with access to biological select agents and toxins should receive training in scientific ethics and dual-use research to foster community responsibility and raise awareness of available institutional support and resources. Federal agencies overseeing and sponsoring select agent research and professional societies should provide educational and training resources to accomplish these goals.

Research on a wide variety of institutional situations and settings shows the importance of having systems or processes in place to support positive action, including monitoring of potential problems among employees. Management plays an essential role and has important responsibilities, such as supporting mechanisms for people to safely self-report problems or concerns about others (for example, ombuds offices, hotlines, confidential reporting systems). Although now largely focused on safety concerns, these processes can serve security goals as well. Occupational



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health and employee assistance programs can also help support monitoring for problems and provide trusted avenues for employees to seek assistance and potentially avoid problems.

Physical Security Based on Risk Assessments

Minimum Requirements

Because each facility is different in design, different physical security approaches are required to address site-specific security requirements. Yet there is inconsistent application of the regulations because of varying interpretations and differing standards. **The Select Agent Program should define minimum cross-agency physical security requirements, which recognize that facilities have unique risk-based security needs and associated design components, to assist facilities in meeting their regulatory obligations.**

Accounting versus Accountability

Accounting for materials and maintaining accurate inventories is essential to keeping biological select agents and toxins out of the wrong hands, but some proposed methods fail to take into account the nature of select agents. **Because biological agents have an ability to replicate, requirements for counting the number of vials or other unreliable measures of the quantity of biological select agents are counter-productive, and lead to a false sense of security. Instead, the report recommends a focus on controlling access to materials: Laboratories should record the identity of all biological select agents as well as toxins, where such materials are stored, who has access and when that access is available, and the intended uses of the materials.**

Inspections

To ensure compliance with current regulations, federal agencies rely on periodic inspections, and some laboratories may be subject to inspections by as many as half a dozen agencies that fund research with biological select agents and toxins in addition to CDC/APHIS. The report recommends steps to streamline these inspections, such as having the

timing coordinated across agencies and operated from a common set of fundamental principles and policies. **The report also recommends that laboratory inspectors have scientific and laboratory knowledge and experience as well as appropriate training specific to biological select agents and toxins research.**

Sustainability

Security and compliance procedures called for under the Select Agent Program can be quite expensive, substantially more than for similar laboratory facilities not conducting biological select agents and toxins research—yet security cannot be compromised. **Federal funding agencies need to provide a separate category of funding to ensure sustained support for biological select agents and toxins facilities.**

Evaluation

Independent evaluation can provide useful information on how the Select Agent Program is implemented and identify important intended and unintended consequences of the program.

The policies and practices of the Select Agent Program should be carefully evaluated, along with the operation of the program overall.

Engaging the Community

To provide continued engagement of stakeholders in oversight of the Select Agent Program, a federal Biological Select Agents and Toxins Advisory Committee should be established. This group would address the need for more systematic communication among agencies funding research with biological select agents and toxins, those administering the Select Agent Program, and those conducting such research. The advisory committee members, who should be drawn from academic/research institutions and the private sector, should include microbiologists and other infectious disease researchers (including select agent researchers), directors of select agent laboratories, and those with experience in biosecurity, animal care and use, compliance, biosafety, and operations. Representatives from the federal agencies with responsibility for funding, conducting, or overseeing select agent research would serve in an *ex officio* capacity.

Committee on Laboratory Security and Personnel Reliability Assurance Systems for Laboratories Conducting Research on Biological Select Agents and Toxins: Rita R. Colwell (*Chair*), University of Maryland, Johns Hopkins University, and CosmosID, Inc.; **Ronald M. Atlas**, University of Louisville; **John D. Clements**, Tulane University; **Joseph A. DiZinno**, BAE Systems; **Adolfo García-Sastre**, Mount Sinai School of Medicine; **Michael G. Gelles**, Deloitte Consulting LLP; **Robert J. Hawley**, Midwest Research Institute; **Sally Katzen**, The Podesta Group; **Paul Langevin**, Merrick and Company; **Todd R. LaPorte**, University of California, Berkeley; **Stephen S. Morse**, Columbia University Mailman School of Public Health; **Kathryn Newcomer**, George Washington University; **Elizabeth Rindskopf Parker**, University of the Pacific; **Paul R. Sackett**, University of Minnesota; **Adam P. Fagen** (Study Director), **Jo L. Husbands**, **Rita Guenther**, and **Carl-Gustav Anderson**, the National Research Council.

The National Academies appointed the above committee of experts to address the specific task in this study, which was sponsored by the National Institutes of Health. The members volunteered their time for this activity; their report is peer-reviewed and signed off by both the committee members and the National Academies.



For more information, contact the Board on Life Sciences at (202) 334-2187 or visit <http://dels.nas.edu/bls/>. Copies of *Responsible Research with Biological Select Agents and Toxins* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.

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