



Responsible Research with Biological Select Agents and Toxins

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Committee on Laboratory Security and Personnel Reliability Assurance
Systems for Laboratories Conducting Research on Biological Select
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Executive Summary

Scientists have been conducting research with the organisms classified as biological select agents and toxins (BSAT) for several hundred years in order to understand the biology of these potentially dangerous pathogens and to develop countermeasures that will diminish the threat they pose. Because of legitimate concerns that BSAT materials might be used in deliberate criminal or terrorist acts, the federal government has instituted policies and procedures governing the security of BSAT laboratories and the reliability of personnel who work with BSAT materials. The committee was asked to consider the appropriate framework for laboratory security and personnel reliability measures that will optimize benefits, minimize risk, and facilitate the productivity of research.¹

The committee identified six principles that should guide consideration of BSAT research; these principles also provide the lens through which the committee offers its conclusions and recommendations:

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.

¹See Box 1-2 for the full statement of task.

Consideration of these principles led the committee to nine recommendations that it believes are essential for keeping BSAT research secure from both internal and external threats.

RECOMMENDATIONS

Recommendation 1 assigns responsibility for fostering a culture of trust and responsibility to a partnership of laboratory leaders and the Select Agent Program:

RECOMMENDATION 1: 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 within BSAT entities. These programs and practices should be designed to minimize potential security and safety risks by identifying and responding to potential personnel issues. These programs should have a number of common elements, tailored to reflect the diversity of facilities conducting BSAT research:

- Consideration should be given to including discussion of personnel monitoring during (1) the initial training required for all personnel prior to gaining access to BSAT materials and annual refresher updates and (2) safety inspections to obtain a more complete assessment of the laboratory's ability to provide a safe and secure research environment.
- More broadly, personnel with access to select agents and toxins should receive training in scientific ethics and dual-use research. Training should be designed to foster community responsibility and raise awareness of all personnel of available institutional support and medical resources.
- Federal agencies overseeing and sponsoring BSAT research and professional societies should provide educational and training resources to accomplish these goals.

Recommendation 2 engages the research community in oversight of the Select Agent Program through formation of an advisory committee:

RECOMMENDATION 2: To provide continued engagement of stakeholders in oversight of the Select Agent Program, a Biological Select Agents and Toxins Advisory Committee (BSATAC) should be established. The members, who should be drawn from academic/research institutions and the private sector, should include microbiologists and other infec-

tious disease researchers (including select agent researchers), directors of BSAT laboratories, and those with experience in biosecurity, animal care and use, compliance, biosafety, and operations. Representatives from the federal agencies with a responsibility for funding, conducting, or overseeing select agent research would serve in an ex officio capacity. Among the responsibilities of this advisory committee should be the following:

- Promulgate guidance on the implementation of the Select Agent Program;
- Facilitate exchange of information across institutions and sectors;
- Promote sharing of successful practices across institutions and sectors;
- Provide oversight for evaluation of the Select Agent Program;
- Provide advice on composition/stratification of the list of select agents and toxins;
- Convene regular meetings of key constituency groups; and
- Promote harmonization of regulatory policies and practices.

Two recommendations address the composition of the list of select agents and toxins and the implications that the nature of the agents has for accountability:

RECOMMENDATION 3: The list of select agents and toxins should be stratified in risk groups according to the potential use of the material as a biothreat agent, with regulatory requirements and procedures calibrated against such stratification. Importantly, mechanisms for timely inclusion or removal of an agent or toxin from the list are necessary and should be developed.

RECOMMENDATION 4: Because biological agents have an ability to replicate, accountability is best achieved by controlling access to archived stocks and working materials. Requirements for counting the number of vials or other such measures of the quantity of biological select agents (other than when an agent is transported from one laboratory site to another) should not be employed because they are both unreliable and counter-productive, yielding a false sense of security. A registered entity should record the identity of all biological select agents and toxins within that entity, where such materials are stored, who has access and when that access is available, and the intended use(s) of the materials.

There have been extensive discussions about the appropriateness of the current Security Risk Assessment process for screening personnel before they

are permitted to work with BSAT; the committee concluded that this process is adequate for screening, but there should be an opportunity to consider mitigating factors as part of an appeal process:

RECOMMENDATION 5: The current Security Risk Assessment screening process should be maintained, but the appeal process should be expanded beyond the simple check for factual errors to include an opportunity to consider the circumstances surrounding otherwise disqualifying factors.

Because of confusion within the community about how physical security requirements should be implemented, the committee calls upon the Select Agent Program to provide a minimum set of requirements that would apply across agencies:

RECOMMENDATION 6: 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.

The committee recognizes the importance of data to inform the operation of the Select Agent Program and recommends ongoing independent evaluation of the program:

RECOMMENDATION 7: Independent evaluation of the Select Agent Program should be undertaken to assess the relative benefits for achieving security, to consider the consequences of the program (intended and unintended) on the research enterprise, and to provide useful data about the Select Agent Program. Such evaluation, which may be coordinated through the BSAT Advisory Committee, should be provided with dedicated funding.

Recognizing the critical role that laboratory inspections play in maintaining the efficient and effective operations of select agent research, the committee calls for appropriate knowledge, experience, and training among inspectors:

RECOMMENDATION 8: Inspectors of select agent laboratories should have scientific and laboratory knowledge and experience, as well as appropriate training in conducting inspections specific to BSAT research. Inspector training and practice should be harmonized across federal, state, local, and other agencies.

Finally, the committee concluded that security and compliance costs have been a challenge for the BSAT research community and calls upon federal funding agencies to provide sustained support for these facility costs:

RECOMMENDATION 9: Because of considerable security and compliance costs associated with research on biological select agents and toxins, federal agencies funding BSAT research should establish a separate category of funding to ensure sustained support for facilities where such research is conducted.

RESPONSIBLE RESEARCH

WITH BIOLOGICAL SELECT AGENTS AND TOXINS

Committee on Laboratory Security and Personnel
Reliability Assurance Systems for Laboratories Conducting
Research on Biological Select Agents and Toxins

Board on Life Sciences

Division on Earth and Life Studies

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Preface

As a scientist who has worked for more than 40 years to find cures for infectious disease, I find the idea that terrorists would use biological agents as a weapon to be anathema. It violates the fundamental values of the life sciences that I and my colleagues hold dear: that science is a vital tool for improving life and the health of our planet and enhancing our understanding of the natural world.

My own work has focused on cholera, a disease responsible for the death of thousands of people around the world every year. During the past 40 years, research carried out through international collaboration of scientists has saved many thousands of lives.

At the same time, we are firm in the belief that this research should be conducted safely and responsibly. The incidence of either laboratory workers or members of the public being infected is vanishingly small, whether from laboratory accidents or intentional action. Through the years, safety and security practices and procedures have been developed that have successfully prevented accidental or intentional misuse of biological materials.

While research with select agents and toxins introduces another level of potential risk, the same sense of responsibility applies. Scientists have not only demonstrated concern about these issues, but also recognize that they have the most at stake should an incident occur. They are best able to identify potential risk, whether from a laboratory door left unsecured or the unusual behavior of a laboratory worker. It is for these reasons that this report focuses on promoting a culture of responsibility, enabling and empowering scientists to be vigilant stewards of their science.

Research with select agents and toxins is both necessary and important. Our nation's health and security depend upon our understanding of these potentially dangerous pathogens and their mechanisms of virulence. Our fundamental

understanding of life and life processes benefits from study of these agents. Nevertheless, there is the possibility that we can be overzealous, implementing procedures only thought to enhance security. While many current policies and practices are effective, some actions suggested to enhance security are not likely to make select agent research more secure, just more difficult to conduct; this may yield the opposite result: that overall security will be diminished, not strengthened.

The authoring committee for this report represents a broad cross-section of stakeholders, including select agent researchers, experts in psychology, professionals in biosafety and facility design, and individuals with extensive experience in the issues of science and security. The report represents a consensus of the committee and our best judgment on the most effective ways to both promote security and foster scientific knowledge and a rapid biological response in the event of an emergency.

With such a challenging task, the committee was given only 3½ months to complete a full report. As such, the committee had to make choices about which issues to address, concentrating on those it felt to be most important, most critical, and most effective for enhancing security and enabling research. Thanks to the dedication of both the committee and staff, analysis of the issues included in the report can be considered no less thorough and documented than if we had been given the luxury of time. The study was conducted at the request of the leadership of the National Interagency Biodefense Campus and the White House Homeland Security Council staff through a contract with the National Institute of Allergy and Infectious Diseases.

On behalf of the entire committee, I wish to extend our sincere gratitude to the excellent staff at the National Academies. This report represents a full year's worth of work conducted in less than four months. It is because of the dedication and extraordinary efforts of study director Adam Fagen, Jo Husbands, Rita Guenther, and Carl-Gustav Anderson that we were able to complete this ambitious task in so short a time. The staff most impressively captured the conclusions of the committee's discussions and ensured access to the information and expertise we needed. The committee was able to identify the most important issues and reach consensus with relative ease because of the superb work of the staff. The tasks were facilitated by a knowledgeable, dedicated, and insightful committee, and I thank my fellow committee members for their commitment that made the study process an enjoyable and rewarding opportunity.

In closing, "every researcher, whether in academia, in government research facilities, or in industry, needs to be aware of the potential unintended consequences of their own and their colleagues' research. In 1975, scientists agreed to the 'Asilomar moratorium,' which gave guidance to researchers in the emerging field of recombinant DNA research. Today, researchers in the biological sciences again need to take responsibility for helping to prevent the potential misuses of their work, while being careful to preserve the vitality of

their disciplines as required to contribute to human welfare.”¹ The committee sincerely hopes that its work will contribute usefully to ongoing discussion of the Select Agent Program and, especially, to the safety and security of select agent research.

Rita R. Colwell, Chair

¹Bruce Alberts and Robert M. May. 2002. Scientist Support for Biological Weapons Controls. *Science* 298(November 8): 1135.

Acknowledgments

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Academies' Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the process.

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by **W. Emmett Barkley**, *Proven Practices LLC*, and **David R. Challoner**, *University of Florida (emeritus)*. Appointed by the National Academies, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

The committee is grateful for those who provided expertise and assistance throughout the study process. This includes those experts who spoke to the committee at one of its meetings: Jeffrey Adamovicz, LouAnn Burnett, Sheldon Cohen, M. Colleen Crowley, Diane Damos, Robert Fein, Kelley Krokos, Bruce Landry, H. Clifford Lane, J. William Leonard, Carol Linden, Richard Meserve, Dennis Metzger, Kevin Murphy, Ben Petro, Mary Rowe, Bryan Vossekuil, Robbin Weyant, and Linda Wilcox. Meeting agendas and speaker affiliations are listed in Appendix B.

The committee is also thankful to those who helped organize or participate in one of the committee's site visits at the New England Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research at Harvard Medical School (Christine Anderson, Gerald Beltz, Mary Corrigan, Robert Dickson, Sara Heninger, Andrew Onderdonk, and Jeff Seo); the MIT Nuclear Reactor Laboratory (John Bernard, David Carpenter, Patricia Drooff, Edward Lau, William McCarthy, Thomas Newton, Jr., and Kathleen O'Connell) and Environmental, Health and Safety Office (Claudia Mickelson) at the Massachusetts Institute of Technology; George Mason University's National Center for Biodefense and Infectious Diseases (Saira Ahmad, Lilian Amer, Charles Bailey, John Blacksten, Calvin Carpenter, Jessica Chertow, Myung Chung, Meghan Durham-Colleran, Suhua Han, Jessica Kidd, Nathan Manes, Beth McKenney, Marjorie Musick, Tony Pierson, Kathleen Powell, Meena Rajan, Ian Reynolds, Diann Stedman, Anne Taylor, Patty Theimer, Monique van Hoek, Anne Verhoeven, Paul Wieber, James Willett, and Ron Witt); and the U.S. Department of Agriculture's National Plant Germplasm and Biotechnology Laboratory (Wayne Claus, Renee DeVries, Joseph Kozlovac, and Laurene Levy). A complete list of site visit participants and affiliations is available in Appendix B.

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