Report of the
Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight

July 2009

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EXECUTIVE SUMMARY

New scientific tools and understanding have created unprecedented opportunities for progress in life sciences research, medicine, and agriculture. Coincident with this era of opportunity have been elevated concerns about emerging infectious diseases, bioterrorism, and criminal acts involving the use of hazardous biological agents, prompting the rapid development of diagnostics, vaccines, and other medical countermeasures. Research on hazardous biological agents that could threaten human health or agriculture has become a national priority, with increased Federal support for programs to promote scientific investigation in academic and commercial settings, as well as in Federal research facilities. Essential to continued progress in these areas of research are the high and maximum containment[1] facilities in which to study these agents.

Effective biosafety and biocontainment practices and oversight of research activities at individual high and maximum containment facilities are critical components of the research enterprise. The Federal Government is committed to the highest quality design and construction of biocontainment facilities, the rigorous training of personnel who work in these laboratories, and the safe conduct of research and research-related activities that occur within these facilities. However, there are areas of concern, which include lapses in biosafety, lack of timely reporting of incidents, and lack of Federal oversight for research involving pathogens that are neither select agents nor recombinant DNA agents. Press reports, articles in scientific publications, Government Accountability Office reports, a report by the Commission on the Prevention of WMD Proliferation and Terrorism,[2] as well as congressional hearings have focused attention on these issues. At the October 4, 2007, House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations hearing entitled "Germs, Viruses, and Secrets: The Silent Proliferation of Bio-Laboratories in the United States," the Department of Health and Human Services (HHS) announced the formation of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (the "Task Force").

Purpose and Scope of the Task Force

[1] The term "high and maximum containment" is used in this report to describe biosafety level 3 (BSL-3) and BSL-4 laboratories and equivalent containment facilities, i.e., animal facility/vivarium ABSL-3 and ABSL-4, and biosafety level-3 agriculture (BSL-3-Ag) facilities. "High containment" refers to BSL-3 and equivalent containment facilities, whereas "maximum containment" refers to BSL-4 and equivalent containment facilities.

[2] The acronym "WMD" refers to weapons of mass destruction. Certain biological agents are regarded as potential WMD.

The purpose of the Task Force is to propose options and recommendations to improve biosafety and biocontainment oversight of research and research-related activities at high and maximum containment laboratories in the United States, without hindering the progress of science.

The scope of activities considered by the Task Force includes those that occur in all high and maximum containment research laboratories in all sectors (government [Federal, State, Tribal, and municipal], academia, privately funded research institutions, and private industry) utilizing potentially hazardous biological agents. The activities covered include research with disease-causing agents (pathogens) that can infect humans, zoonotic agents that can infect both animals and humans, biologic toxins, and agricultural pathogens and pests. Also included are activities related to research, such as the maintenance of facilities and equipment needed for effective biosafety and biocontainment, incident-reporting, and public outreach and communication efforts.

Outside the scope of the Task Force report are non-research activities that take place in diagnostic and treatment (non-research) facilities such as hospitals, clinics, veterinary, and food diagnostic laboratories. Non-research activities in most licensed biomedical production facilities and mobile field analytical laboratories also lie outside the scope of this report because they vary markedly from those of facilities engaged in high and maximum containment research.

To generate this report, the Task Force reviewed the current system of biosafety and biocontainment oversight by individual research institutions, a sampling of municipal and State government entities, and Federal agencies.[3] The review included oversight entities, processes, and mechanisms; Federal regulations, guidelines, standards, and policies; and mechanisms for coordinating oversight activities. In addition, the Task Force discussed the accountability and compliance of individuals and institutions; training and competency of relevant staff at high and maximum containment research institutions; incident-reporting, analysis, and information-sharing; maintenance of facility infrastructure and equipment; applied biosafety research programs; and public communication, outreach, and transparency.

The issues of biosecurity and personnel reliability, although related to laboratory biosafety and biocontainment, are not the focus of this report but are being addressed by a Federal Working Group established by Executive Order 13486, *Strengthening Laboratory Biosecurity in the United States*. All three issues—biosafety/biocontainment, biosecurity, and personnel reliability—are important and are being explored in detail by the Federal Government.

[3] Although the Task Force reviewed oversight at many levels, its emphasis is on Federal and "local" biosafety/biocontainment oversight of research and related activities at high and maximum containment facilities. In this report, the term "local oversight" refers to oversight of the biosafety/biocontainment entities, processes, and mechanisms in place at facilities where high or maximum containment research is conducted.

Membership of the Task Force

The Task Force is co-chaired by HHS and the U.S. Department of Agriculture (USDA), and is comprised of representatives from a broad range of Federal agencies that have responsibility for and oversight of work with hazardous biological agents at high and maximum containment research facilities. In addition to HHS and USDA, the members of the Task Force include representatives from the Departments of Commerce, Defense, Energy, Homeland Security, Labor, State, Transportation, Veterans' Affairs, as well as the Environmental Protection Agency and National Science Foundation.

Importance of Public Involvement

Given the importance of laboratory biosafety and biocontainment to many private-sector research activities, as well as to the protection of laboratory workers, public health, agriculture, and the environment, input from key stakeholders in academia, private industry, and professional societies, as well as the public at large, is critical. To that end, the Task Force held a public engagement meeting on December 8−9, 2008.

Importance of High and Maximum Containment Research

The need for strategies and products to protect public health and agriculture in the event of a natural emergency, man-made biological incident or event, or act of bioterrorism has resulted in the growth of research programs across the Federal Government. Critical to the increased need for research is the necessity of developing a nationwide system of infrastructure that supports the research enterprise. Important components of this infrastructure are the high and maximum containment research laboratories that are the focus of this report. The Federal departments most engaged in research to protect human health and the food supply are HHS and USDA. Other Federal departments and strategic partners in academia and private industry also play critical roles.

Despite remarkable scientific progress, infectious diseases exact an enormous toll on public health, animal and plant health, and agriculture. Bacteria, viruses, and other disease-causing organisms continue to emerge and evolve due to a range of factors including changes in human demographics, human behavior, and land use. In addition to the continuing challenge posed by infectious disease, the dissemination of *Bacillus anthracis* (anthrax) spores through the U.S. mail in the fall of 2001 prompted the Federal Government, with bipartisan support from Congress, to increase dramatically the nation's investment in the development of medical countermeasures to protect the public against biological agents that could be used in terrorist or criminal acts.

Brief Summary of the Evolution of Biosafety and Biocontainment Practices

Work with infectious agents in the laboratory always involves risk; Federal, State, Tribal, and municipal entities, as well as scientists and individual research institutions, have taken numerous steps to mitigate those risks. The development of biosafety and biocontainment practices and procedures, as well as programs to train professionals who oversee biosafety/biocontainment management programs at individual research institutions, has paralleled the development of the science of microbiology and its extension into new and related areas such as tissue culture, recombinant DNA (rDNA) technology, and the use of animals and plants in research and biotechnology. Many of the biosafety/biocontainment practices and procedures in use today resulted from the pioneering efforts of U.S. scientists at Fort Detrick in the 1950s and 1960s. Since then, Federal agencies have published and updated biosafety/biocontainment guidelines, standards, regulations, and policies designed to protect laboratory workers, public health, animal and plant health, agriculture, and the environment.

Current Framework for Biosafety and Biocontainment Oversight

Multiple, complementary, and sometimes overlapping biosafety and biocontainment oversight requirements exist within the Federal government; among Federal, State, Tribal, and municipal governments; and among various levels of government and individual research institutions. The redundancy in the biosafety and biocontainment framework helps ensure the protection of laboratory workers, public health, animal and plant health, the food supply, and the environment from exposure to hazardous biological agents and toxins used in laboratories. The individual elements of biosafety and biocontainment oversight vary, depending on the facilities and activities that require oversight, and the numerous government agencies and local institutions that play roles in particular oversight activities.

The Federal entities that have primary regulatory oversight responsibility for high and maximum containment research facilities are the Department of Labor (DOL), Occupational Safety and Health Administration (OSHA), HHS Centers for Disease Control and Prevention (CDC), and the USDA Animal and Plant Health Inspection Service (APHIS). The biosafety/biocontainment regulations, requirements, and guidelines most relevant to research involving biohazards at high and maximum containment laboratories are the OSHA *General Duty Clause*, *Bloodborne Pathogens Standard*, and *Personal Protective Equipment Standards*; HHS and USDA *Select Agent Regulations*; USDA regulations that require permits for work with high-consequence animal and plant pathogens; CDC regulations that require a permit for the import of any infectious agent known or suspected to cause disease in humans; the NIH and CDC guidance document entitled *Biosafety in Microbiological and Biomedical Laboratories*; and the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*).

Vision, Guiding Principles, and Ultimate Goal

Vision of the Trans-Federal Task Force

The Task Force envisions that a national system for biosafety and biocontainment oversight of high and maximum containment research should achieve effective, comprehensive oversight at individual institutions where the research is conducted (local oversight) and at the Federal level. Local and Federal oversight should be executed in a manner that protects laboratory personnel, public health, plant and animal health, agriculture, and the environment while fostering the progress of research.

Guiding Principles

The guiding principles identified below apply to all aspects of the system for biosafety and biocontainment oversight of research and related activities at high and maximum containment facilities in all sectors.

- Research on hazardous biological agents (pathogens and toxins) that requires high and maximum containment facilities is vital for ensuring public and agricultural health. This research contributes significantly to the understanding of human, plant, and animal pathogens and the diseases they cause; the development of new diagnostics, treatments, and preventive measures for protecting human, plant, and animal health; the development of a more robust and nutritious food supply; and the development of medical countermeasures for biodefense.

- Biosafety and biocontainment oversight must ensure the safe conduct of research without creating undue impediments to scientific progress. Rigorous adherence to biosafety and biocontainment standards and practices by all individuals and institutions involved in high and maximum containment research is essential to protecting laboratory personnel, public health, plant and animal health, agriculture, and the environment. At the same time, it is critical that oversight measures allow important scientific research to proceed efficiently, and ensure sufficient flexibility so that new challenges to public health or agriculture, or emergency situations, can be addressed quickly and effectively.

- Local oversight is key to effective biosafety and biocontainment. The foundations of an effective and comprehensive system of biosafety and biocontainment oversight are the personnel, processes, and procedures in place at individual research institutions.

- Transparency and accountability are critical to the success of high and maximum containment research, as well as biosafety and biocontainment oversight of these research activities. Achieving transparency and accountability requires effective outreach and communication with the scientific community and the public.

- Periodic evaluations are essential to ensure effective oversight. There is a need for periodic and thorough evaluation of all components of laboratory biosafety and biocontainment oversight systems in place at all levels—from individual research

institutions to the Federal Government—to ensure their effectiveness. The process of optimizing biosafety and biocontainment oversight must evolve as needs change.

Ultimate Goal

The ultimate goal is to optimize biosafety and biocontainment oversight of research and related activities in high and maximum containment laboratories in all sectors by developing a coordinated and synergistic approach that does not impede the scientific enterprise.

Objectives and Recommendations

Despite the comprehensive nature of current biosafety and biocontainment oversight of high and maximum containment research, the Federal Government recognizes that the oversight framework could be enhanced, and would benefit from a more formalized and systematic approach that includes uniformly applied standards. To that end, the Task Force analyzed the current framework for biosafety and biocontainment oversight, identified eight areas in which oversight could be improved, and defined eight objectives to address these areas. In the report that follows, each objective is described together with specific issues, options for addressing the objective, and recommendations of the Task Force.

In the short term, many recommendations (1) require compliance and implementation by institutions that are Federally owned or funded by the Federal Government; and (2) encourage compliance by individuals and institutions not Federally owned or receiving Federal support. In the long term, these recommendations should lead to a comprehensive national strategy for biosafety and biocontainment oversight, and compliance and implementation by all individuals and institutions in all sectors. The Task Force recognizes that its recommendations also could be applied to entities outside the scope of this report, and that legislation or rulemaking might be required to implement the recommendations in all sectors.

These recommendations were developed without consideration of potential competing priorities across the Federal Government, and their implementation would be subject to the availability of funds.

SUMMARY OF OBJECTIVES AND TASK FORCE RECOMMENDATIONS

OBJECTIVE 1: Enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research through improved coordination of oversight activities.

Recommendations:

- **1.1: Identify or establish a Federal entity to coordinate biosafety and biocontainment oversight activities, and to ensure comprehensive and effective Federal oversight for all high and maximum containment research facilities and activities in all sectors.**
- **1.2: Develop a registry of all high and maximum containment research facilities in the United States.**
- **1.3: Require that all institutions conducting high and maximum containment research designate: (1) a senior official with the appropriate knowledge, authority, and accountability who is responsible for institutional compliance with biosafety and biocontainment regulations and guidelines; and (2) a credentialed biosafety professional (see Recommendation 3.3) who is responsible for oversight of biosafety and biocontainment programs.**
- **1.4: Require that, at all institutions conducting high or maximum containment research, an appropriately constituted review body performs a thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment.**

OBJECTIVE 2: Encourage a robust culture of accountability characterized by individual and institutional compliance with biosafety and biocontainment regulations, guidelines, standards, and policies.

Recommendations:

- **2.1: Mandate compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.**
- **2.2: Support the development of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions.**

OBJECTIVE 3: Develop a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories.

Recommendations:

- **3.1: Establish national, position-specific training standards and core competencies in biosafety and biocontainment for all research, managerial, and support personnel at high and maximum containment research laboratories in all sectors.**
- **3.2: Require institutions to ensure that all individuals who work in, oversee, support, or manage high or maximum containment research laboratories are appropriately trained and competent in biosafety and biocontainment.**
- **3.3: Implement a phased-in requirement that the designated biosafety professional (Biological Safety Officer or equivalent) at all high and maximum containment research facilities be credentialed.**

OBJECTIVE 4: Obtain and analyze information about laboratory incidents to enable trend analysis, minimize the number of future incidents, and share lessons learned, with the overall goals of optimizing laboratory safety and oversight.

Recommendation:

- **4.1: Establish: (1) a new voluntary, non-punitive incident-reporting system for high and maximum containment research laboratories that would ensure the protection of sensitive and private information, as necessary; and (2) a centralized, integrated mechanism for analyzing incidents and sharing information and lessons learned from both current mandatory reports and the new voluntary reporting system**

OBJECTIVE 5: Ensure that biosafety and biocontainment regulations and guidelines cover current and emerging hazardous biological agents, and develop an agricultural equivalent of the *BMBL*.

Recommendations:

- **5.1: Develop comprehensive biocontainment guidelines comparable to those of the *BMBL* to cover research, including high and maximum containment research, on plant, livestock, and other agriculturally significant pests and pathogens.**
- **5.2: Maintain rigorous and comprehensive processes for the review and updating of biosafety and biocontainment regulations and guidelines, and ensure that these processes include broad-based participation by all relevant stakeholders.**

OBJECTIVE 6: Ensure that the infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained.

Recommendations:

- **6.1: Require that all institutions with high or maximum containment laboratories ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment.**
- **6.2: Develop a mechanism for sharing information and best practices about infrastructure and equipment design, operations, and maintenance among all high and maximum containment research facilities.**

OBJECTIVE 7: Develop and support a national research agenda for applied biosafety and biocontainment to improve the management of biohazard risks.

Recommendation:

- **7.1: Develop and maintain a robust program of applied biosafety and biocontainment research to create additional and update existing evidence-based practices and technologies.**

OBJECTIVE 8: Improve and share strategies to ensure effective public communication, outreach, and transparency about biosafety and biocontainment issues.

Recommendation:

- **8.1: Develop comprehensive strategies to improve public communication, outreach, and transparency about biosafety and biocontainment issues and activities at high and maximum containment research facilities.**

Conclusion

There is a robust system for laboratory biosafety and biocontainment oversight in place. The objectives and recommendations in this report are designed to optimize local biosafety and biocontainment oversight at individual high and maximum containment research facilities; improve and better coordinate Federal oversight of these facilities and their activities; and help increase public confidence and trust that high and maximum containment research laboratories in the United States are being operated as safely as possible.

Acting on the objectives and recommendations in this report will require enhanced communication and collaboration among Federal entities and their non-Federal partners, and, in some cases, addition or redirection of resources, as well as further analysis.

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I. OVERVIEW AND CHARGE OF THE TRANS-FEDERAL TASK FORCE ON OPTIMIZING BIOSAFETY AND BIOCONTAINMENT OVERSIGHT

New scientific tools and understanding have created unprecedented opportunities for progress in life sciences research, including discoveries of the molecular mechanisms by which certain microbes cause disease, and the means by which new infectious disease threats can emerge. These opportunities can enable many important advances in medicine, public health, and agriculture. Coincident with this era of opportunity have been elevated concerns about infectious diseases and bioterrorism, as well as criminal acts involving the use of biological agents, giving rise to an urgent need for the rapid development of diagnostics, vaccines, and other biodefense-related medical countermeasures. Research into these areas has become a national priority, with increased Federal support for programs to promote scientific investigation in academic and commercial settings, as well as in Federal research facilities.

The importance of effective biosafety and biocontainment practices and oversight of activities involving work with potential biological hazards (infectious disease-causing organisms and biological toxins) at individual research institutions and Federal agencies cannot be overemphasized. Although the Federal Government is committed to ensuring the highest quality design and construction of high and maximum containment facilities, the rigorous training of personnel who work in them, and the safe conduct of research undertaken in them, there are areas of concern. Press reports, articles in scientific publications,[4] Government Accountability Office reports,[5,6] and a report by the Commission on the Prevention of WMD Proliferation and Terrorism,[7] as well as congressional concerns have focused attention on the issues of biosafety and biosecurity[8] at high and maximum containment laboratories.

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[4] Kaiser J. Biosafety Breaches: Accidents spur a closer look at risks at biodefense labs. *Science*. 2007. 317 (5846):1852-1854.

[5] U.S. Government Accountability Office. *HIGH-CONTAINMENT BIOSAFETY LABORATORIES, Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*. 2007. GA0-08-108T.

[6] U.S. Government Accountability Office. *Biosafety Laboratories: Perimeter Security Assessment of the Nation's Five BSL-4 Laboratories*. 2008. GAO-08-1092. HHS/CDC has provided corrections to the GAO preliminary report but a revised, corrected version had not been published as of June 2009.

[7] *World at Risk: The Report of the Commission on the Prevention of WMD Proliferation and Terrorism*. Released December 2, 2008. See http://www.preventwmd.gov/report/.

[8] Executive Order 13486, signed on January 9, 2009, by former President George W. Bush, ordered the establishment of the Working Group on Strengthening the Biosecurity of the United States. The working group was charged with preparing a report on laboratory biosecurity and personnel reliability, topics that are related to biosafety. Executive Order 13486 is available at http://fas.org/irp/offdocs/eo/eo-13486.htm.

On October 4, 2007, the House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, held a hearing entitled "Germs, Viruses, and Secrets: The Silent Proliferation of Bio-Laboratories in the United States."[9] At the hearing, subcommittee members voiced concerns about what they viewed as the risks associated with the proliferation of high and maximum containment laboratories (biosafety level 3 [BSL-3] and biosafety level 4 [BSL-4] and their agricultural equivalents) in the United States. At issue was the status of Federal oversight of BSL-3, BSL-4, and equivalent agricultural containment facilities, including the number and locations of all BSL-3 facilities. (The number and locations of U.S. BSL-4 facilities are known.)

At the October 2007 hearing, agency representatives from the U.S. Department of Health and Human Services (HHS) announced the establishment of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force). The Task Force was established to undertake an intensive analysis of the current framework of biosafety and biocontainment oversight of high and maximum containment research on hazardous biological agents and toxins, with the goal of exploring strategies to address concerns voiced by Congress and the general public.

The Task Force is chaired by officials from HHS and the U.S. Department of Agriculture (USDA), and is comprised of representatives from a broad range of Federal departments and agencies that have responsibility for, and oversight of the management of biohazard risks. Included in the Task Force are members from HHS, USDA, and the Departments of Commerce, Defense, Energy, Homeland Security, Labor, State, Transportation, and Veterans' Affairs as well as the Environmental Protection Agency and the National Science Foundation (see Appendix A).

Task Force Charge and Vision

The purpose of the Task Force is to propose options and recommendations to improve biosafety and biocontainment oversight of research activities at high and maximum containment research laboratories in the United States through a comprehensive review of mechanisms by which individual research (local) institutions and the Federal Government can ensure safe working conditions (see Appendix B). The Task Force envisions effective, comprehensive, local (institutional) and Federal oversight that protects laboratory workers, public health, plant and animal health, agriculture, and the environment, without hindering the progress of science. The Task Force was charged to present this report to the USDA and HHS Secretaries for their consideration.

Definitions of Key Terms Used in the Report

[9] For testimony and information about the October 4, 2007, congressional hearing, see http://energycommerce.house.gov/index.php?option=com_content&task=view&id=105&Itemid=93.

"Biosafety" refers to the application of combinations of laboratory practices and procedures, laboratory facilities, safety equipment, and appropriate occupational health programs when working with potentially infectious microorganisms and other biohazards.[10] Current biosafety and biocontainment practices and procedures are designed to reduce the exposure of laboratory personnel, the public, agriculture, and the environment to potentially infectious agents and other biological hazards. The key principles of biosafety are risk assessment and containment. The principles of biosafety and biocontainment have been articulated in two key reference documents, the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (first published in 1976), and the CDC and NIH manual entitled *Biosafety in Microbiological and Biomedical Laboratories (BMBL*, initially issued in 1984). These documents have been amended and revised over the years to reflect advances in science and technology. The current (fifth) edition of the *BMBL* was released online in 2007.[11] For more than two decades, the *BMBL* has been the code of practice for biosafety and biocontainment in the United States.

The term "biocontainment" is used differently in facilities for the study of human pathogens versus those used for the study of agricultural pathogens. In agricultural facilities, the definition for "biocontainment" resembles that for "biosafety," i.e., the safety practices and procedures used to prevent unintended infection of plants or animals or the release of high-consequence pathogenic agents into the environment (air, soil, or water). However, for all high and maximum containment facilities, "biocontainment" also refers to the physical containment barriers in a facility such as contained dressing and shower rooms, sealed service penetrations, specialized doors, entry and exit avenues to prevent cross-contamination, specialized air handling systems for contamination control, personal protective equipment, biosafety cabinets, etc. In the agricultural setting**,** worker protection and public health are always considerations; however, emphasis is placed on reducing the risk that agents under study could escape into the environment. The development of risk-assessment and management methods for agricultural biohazards differ from those that focus on risks to public health and laboratory workers, in that the primary risk-assessment drivers for agricultural biohazards are the economic impact of animal and plant morbidity and mortality, and the trade implications of disease.

"Biosafety levels" (BSL) are designations of laboratories in ascending order based on the degree of risk associated with the work being conducted. The designations BSL-1, BSL-2, BSL-3, and BSL-4 are for work with human and zoonotic pathogens and are based on the utilization of combinations of engineering controls, facility design, safe work practices, and safety equipment. Each combination is specifically appropriate for the operations performed, the documented or suspected routes of transmission of the infectious agents, and the laboratory function or activity. The assignment of a biosafety level to a particular work process or research protocol is made through protocol-driven risk assessment so that potential hazards specific to the work can be identified and

[10] Adapted from CDC definition available at http://www.cdc.gov/od/ohs/pdffiles/Module%202%20-%20Biosafety.pdf.

[11] For the online fifth edition of the *BMBL*, developed by the U.S. National Institutes of Health and the Centers for Disease Control and Prevention, see http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm.

mitigated effectively. The "BSL" term for laboratory designation does not apply to plant pathogens. However, plant pathogens are typically contained in laboratories and greenhouse facilities with containment features similar to those described for BSL-1, BSL-2 and BSL-3 laboratories.

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

Scope of Activity

The scope of research activities considered by the Task Force includes those that occur in all high and maximum containment laboratory research facilities in all sectors (Federal, State, academic, private, and commercial laboratories) utilizing potentially hazardous biological agents (pathogens and toxins). (For a table showing the scope of Federal regulations, guidelines, and oversight entities, see Appendix C.)

Beyond the scope of the Task Force report are non-research activities that take place in diagnostic and treatment (non-research) facilities such as hospitals, clinics, veterinary, and food diagnostic laboratories. These include some laboratories associated with the National Animal Health Laboratory Network (NAHLN) and the Food Emergency Response Network (FERN). Non-research activities in most licensed biomedical production facilities and mobile field analytical laboratories also lie outside the scope of this report because they are not research facilities. The activities of these facilities vary markedly from those engaged in high and maximum containment research.

Although this report offers a brief discussion of the relationship between laboratory biosecurity and biosafety, laboratory biosecurity *per se* is not the focus of this report. The term "laboratory biosecurity" denotes the protection of hazardous biological agents, including toxins, from loss, theft, diversion, or intentional misuse. Good biosafety and biocontainment practices contribute to effective laboratory biosecurity, and the disciplines of biosafety and laboratory biosecurity are complementary in many aspects. However, the Task Force did not want to deviate substantially from its focus on biosafety and biocontainment oversight.

Approach

In developing the report, the Task Force focused on:

- Conducting a comprehensive assessment of the current biosafety/biocontainment oversight framework for high and maximum containment laboratory research activities and facilities in all sectors. Oversight is achieved at many levels, the most critical of which are individual research institutions ("local oversight") and Federal entities such as HHS/CDC and USDA/APHIS ("Federal oversight"). The Task Force review encompassed the identification and assessment of pertinent laws, regulations, policies, standards, and guidelines in addition to examining current biosafety/biocontainment oversight mechanisms in use by local institutions as well as municipal, State, and Federal oversight entities.

- Developing specific objectives for improving the current biosafety/biocontainment oversight framework. The objectives are based on identifying issues and needs related to the current biosafety/biocontainment oversight framework for high and maximum containment laboratories in which research on hazardous biological agents is conducted.

- Developing options and recommendations for achieving the objectives. In efforts to explore strategies that best meet the biosafety and biocontainment needs of Federal and non-Federal research involving biological hazards, Task Force members endeavored to strike a balance among solutions to optimize biosafety and biocontainment oversight and the potential impact of increased oversight. **The focus was on devising a framework that improves biosafety and biocontainment oversight, incident-reporting, and training without causing unintended negative consequences for progress in research.**

The Task Force's process of deliberation and consultation also included soliciting the perspectives and input from key stakeholders. A public consultation meeting was held December 8−9, 2008. Based on input from those who attended the meeting or submitted comments to the website established for that purpose, the Task Force further developed and revised this report.

Engaging the public as a key stakeholder is vital given the critical importance of biosafety and biocontainment oversight for protecting laboratory workers, public health, agriculture, and the environment. Public engagement also is critical to address the concerns of communities in which high and maximum containment facilities are located or planned, because of public perception that these facilities could adversely affect public health or the environment. The Task Force recognizes that extensive consultation with the researchers, biosafety professionals, and science administrators responsible for high and maximum containment research facilities also is crucial for implementing measures to enhance the existing framework for biosafety and biocontainment oversight, and for ensuring the measures are appropriate, practical, and acceptable.

Continued strengthening of biosafety/biocontainment oversight of research at high and maximum containment facilities in all sectors will require informed action on the part of the Federal Government; State and municipal authorities; experts in biosafety and

biocontainment; scientists; professional organizations; and the public. It is the expectation of the Task Force that its recommendations will lead to the development and implementation of an optimized framework for biosafety and biocontainment oversight.

II. BACKGROUND

Introduction

The background information provided in this chapter is designed to help set the stage for the objectives, options, and recommendations developed by the Task Force, and the further evolution and refinement of biosafety and biocontainment practices and oversight. This chapter addresses three major topics: (1) the importance of high and maximum containment laboratory research; (2) a brief history of biosafety and biocontainment practices and procedures; and (3) public and congressional concerns about the oversight of biosafety level (BSL)-3 (high containment), BSL-4 (maximum containment), and equivalent containment facilities used in agricultural research.

Importance of High and Maximum Containment Laboratory Research

Developing measures to protect public health and agriculture against biological threats, whether due to natural causes or deliberate release, will continue to be a high priority of national security for the foreseeable future. Critical to the increased need for research is a nationwide system of infrastructure that supports the research enterprise. Important components of this infrastructure are the high and maximum containment research laboratories that are the focus of this report. Individual Federal agencies play specific roles in research at BSL-3, BSL-4, and equivalent agricultural containment facilities. Academic institutions and private industry also have accelerated high and maximum containment research, in part to develop products and technologies to protect public health and the food supply.

Just as the investment in HIV/AIDS research advanced the understanding and treatment of many other diseases, the advancement of knowledge gained through research at high and maximum containment facilities is enhancing the ability to diagnose, treat, and prevent important diseases such as tuberculosis (TB) and plague, as well as emerging and re-emerging infectious diseases such as severe acute respiratory syndrome (SARS), dengue, and hemorrhagic fevers caused by Ebola and Marburg viruses. Similarly, high containment agricultural research (equivalent to BSL-3) on livestock and crop pathogens, including high-consequence animal diseases (e.g., foot-and-mouth disease and highly pathogenic H5N1 avian influenza virus), plant pathogens (bacteria, viruses, fungi, and parasites), and pests, as well as invasive plant species leads to improved methods of protecting U.S. agriculture and the food supply.[12]

The need for strategies and products to protect public health and agriculture in the event of a natural emergency, accidental breach of containment, or bioterrorism event has

[12] Maximum containment (equivalent of BSL-4) is used in agricultural research only for zoonotic agents that can infect both animals and humans.

resulted in the growth of biodefense research programs supported by the Federal government,[13] which include research activities, and many related activities such as infrastructure development, training, and biosecurity measures.

Emerging and Re-emerging Infectious Diseases: Impact on Human Health

Despite remarkable advances in medical research and the development of medical products (diagnostics, treatments, vaccines, and other preventive measures) during the 20th century, infectious diseases remain a leading cause of death worldwide for three primary reasons: the emergence of new infectious diseases, the re-emergence of infectious diseases that previously have affected humans, and the persistence of intractable infectious diseases.[14]

Various factors affect the spread and evolution of infectious diseases. Changes in human demographics, human behavior, and land use are contributing to the emergence of new human and zoonotic diseases by bringing people into closer and more frequent contact with pathogens, for example, through exposure to animal or arthropod carriers of disease. Increasing trade in exotic animals for pets and as food sources also has contributed to the increased opportunities for pathogens to jump from animal reservoirs to humans. For instance, close contact with exotic rodents imported as pets to the United States was found to be the origin of the 2003 U.S. outbreak of monkeypox,[15] and the use of exotic civet cats for meat in China was found to be the route by which the SARS coronavirus made the transition from its natural reservoir to susceptible human hosts.[16]

At the same time, infectious diseases once effectively managed through prevention measures and treatment are "re-emerging" as public health threats among various human populations. The pathogens that cause some of these diseases are studied in high and maximum containment laboratories. Natural genetic variations and adaptations allow new strains of known pathogens to appear in forms the human immune system is not primed to recognize (e.g., seasonal influenza or the recently identified novel HIN1 influenza virus). Furthermore, increased and sometimes imprudent use of antimicrobial drugs and pesticides has led to the emergence of drug-resistant pathogens, allowing many diseases that formerly could be treated to occur in a far more hazardous form (e.g., multidrug-resistant and extensively drug-resistant tuberculosis [MDR-TB and XDR-TB] and various foodborne infections). Recently, decreased compliance with vaccination policies also has led to the resurgence of childhood diseases that previously were under control.

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[13] Franco C. Billions for Biodefense: Federal Agency Biodefense Funding, FY 2008–FY 2009**.** *Biosecurity and Bioterrorism*. 2008. 6(2): 131-146.

[14] For more information about research on emerging and re-emerging infectious diseases, see http://www3.niaid.nih.gov/research/topics/emerging/introduction.htm.

[15] See CDC Interim Final Rule, "Control of Communicable Diseases; Restrictions on African Rodents, Prairie Dogs, and Certain Other Animals," banning the importation of African rodents into the United States, available at http://edocket.access.gpo.gov/2003/03-27557.htm, and update at http://www.cdc.gov/nciDOD/monkeypox/animals.htm.

[16] Guan Y, et al. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. *Science*. 2003. 302(5643): 276-278.

Infectious Diseases and Pests: Impact on Animal and Plant Health and the Food Supply

The system of U.S. agriculture is the largest and most extensive in the world. It is the largest industry and employer in the United States, generating more than $1 trillion in economic activity annually, including more than $50 billion in exports.[17] The introduction of animal and plant diseases to farms, and pathogens to the food supply would cause severe economic disruption, given that agriculture accounts for 13 percent of the U.S. gross domestic product and 18 percent of domestic employment.[18] Losses to farmers could result from decreases in the price of livestock, poultry, and crops; reductions in sales due to a decline or halt in productivity and the loss of international markets; the inability to move animals to market; and costs associated with disease control, including the disposal of affected animals or plants.

Infectious organisms also threaten the safety of the food supply. Several new livestock and crop diseases emerge each year. Globalization of trade, movement of masses of people and agricultural products, changing weather patterns, rapid population growth in cities, intensive and interconnected agriculture systems, limited genetic diversity in farm animals, changes in farm practices—all these factors are creating new opportunities for the emergence, re-emergence, and spread of infectious agricultural diseases and pests throughout the United States, thus underscoring the continued and critical need for research in these areas.

Threats to agriculture include foreign animal diseases (FADs), which are defined as animal diseases that never have been present in the United States or that were eradicated through intensive and expensive control programs. Most animals in the United States are not vaccinated against many FADs and therefore are susceptible to infection with these agents. Recent outbreaks in other countries have shown that certain FADs, such as foot-and-mouth disease, can move rapidly from one farm to another via infected animals or contaminated equipment. Intensive, modern agricultural practices promote high-density livestock populations that are bred and reared in close proximity. The outbreak of a contagious FAD at one such facility would be difficult to contain, particularly if the disease were transmitted though an airborne route.

The United States has a long history of success in eradicating many serious animal diseases, largely through cooperation between the U.S. Department of Agriculture (USDA) agencies and affected states. In addition, the United States has collaborated with many countries, particularly those in the Americas, to eradicate serious animal diseases, thus lowering the risk of FADs that cross U.S. borders. However, the ever-present risk

[17] U.S. Government Accountability Office. 2005. Report to Congressional Requesters. Homeland Security. *Much is Being Done to Protect Agriculture from a Terrorism Attack, but Important Challenges Remain.* GAO-05-214. Washington, D.C.

[18] U.S. Government Accountability Office. 2003. *Bioterrorism: A Threat to Agriculture and the Food Supply.* GAO-04-259T. Testimony Before the Committee on governmental Affairs, US, U.S. Senate Statement for the Record by Lawrence J. Dyckman, Director Natural Resources and Environment, Washington, D.C.

remains for the accidental introduction of an agriculturally significant pathogen or pest due to increased global travel and trade.

Threat of Bioterrorism and Agroterrorism: Congressional Support to Fund New Research Programs to Address Terrorist Threats

The dissemination of *Bacillus anthracis* (anthrax) spores through the U.S. mail in the fall of 2001 coupled with emerging and re-emerging infectious diseases, and the need to protect the food supply from naturally occurring or deliberate threats, prompted the Federal Government, with bipartisan support from Congress, to increase dramatically spending on biodefense research, with the specific goal of developing medical countermeasures to protect public health and agriculture. Many biodefense research activities, including those that involve high-consequence agricultural pathogens and toxins, are conducted in high and maximum containment facilities.

- Federal entities involved in research to address terrorist threats. The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), supports and oversees a broad program that includes basic research and the development of new and improved products for the prevention, diagnosis, and treatment of diseases caused by emerging and re-emerging infectious diseases, including potential agents of bioterrorism. NIAID has set research priorities and goals for each known microorganism that might be used as an agent of bioterrorism.

  The Biomedical Advanced Research and Development Authority (BARDA), an office of the HHS Assistant Secretary for Preparedness and Response, is charged with the advanced research, development, and procurement of medical countermeasures for biological, chemical, and radiological/nuclear threats, as well as for emerging and re-emerging infectious diseases such as pandemic influenza.

  The Centers for Disease Control and Prevention (CDC) also received significant funds to develop a national response to acts of bioterrorism. Much of the funding has been used to develop State and local readiness to respond to attacks using biological agents; however, significant investments also have been made in areas of applied research, diagnostic development, and methods to characterize agents used in these events. Detection assays developed at CDC have been deployed through a laboratory network, the Laboratory Response Network (LRN), to more than 150 laboratories throughout the United States and a few laboratories in international locations. The vast majority of these facilities are public health laboratories at the State and local levels.

  The USDA Agricultural Research Service (ARS), through its "farm to fork" research program, helps ensure the safety of food, from production through processing, preparation, and consumption. The system of food production and distribution in the United States is diverse, extensive, and easily accessible and is

susceptible to the introduction of pathogens, bacterial toxins, fungal toxins (mycotoxins), and chemical contaminants through natural processes, global commerce, and intentional means. In response to these threats, crop and livestock production systems must be protected from pathogens, toxins, and chemicals that cause disease in humans. To ensure the security of production systems, ARS conducts basic, applied, and developmental research resulting in new technologies, new and improved management practices, pest-management strategies, sustainable production systems, and methods of controlling potential contaminants.

The tools developed by ARS assist other USDA agencies including the Animal and Plant Health Inspection Service (APHIS) and the Food Safety and Inspection Service (FSIS) to fulfill their roles in protecting U.S. agriculture and the food supply. APHIS provides leadership to ensure the health and care of animals and plants; the agency also has oversight responsibility for high and maximum containment agricultural research facilities. FSIS monitors the safety of the food supply, and develops, adapts, and validates threat agent detection methods for foods. FSIS also provides funding to State and local food-testing laboratories to participate in method development and validations for threat agent detection methods.

The Department of Homeland Security (DHS), through its National Biodefense Analysis and Countermeasures Center, supports research on understanding biological threat agents and developing the forensic tools to support analysis and investigation of acts of bioterrorism and crimes using biological agents.

The Department of Defense (DOD), through its longstanding Chemical and Biological Defense Program, supports research on biological threats and the development of countermeasures against those threats. DOD research activities occur at numerous facilities, including military laboratories as well as those supported by contracts in academia and private industry.

Subsequent to the 2001 mailing of letters containing spores of *Bacillus anthracis*, the role of the Environmental Protection Agency (EPA) with respect to homeland security was expanded. Presidential Directives identified EPA as the primary Federal agency responsible for protection and remediation of public water supplies following an attack on indoor or outdoor areas. In recognition of this expanded role, EPA established a homeland security research program charged with developing and delivering reliable, responsive expertise and products based on scientific research and evaluations of technology.

- Federal funding for research and infrastructure, including high and maximum containment research laboratories. Because there has been an increased need for research on emerging and re-emerging infectious diseases and civilian biodefense, Federal funding for these activities has increased since 2003. Critical to the increased need for research is a nationwide system of infrastructure that supports

the research enterprise. Important elements of this infrastructure are the high and maximum containment research laboratories that are the focus of this report. Individual Federal departments and agencies play specific roles in these research activities, and their budgets have increased accordingly.

Brief History of Biosafety and Biocontainment Practices and Procedures

The development of the profession and tenets of biosafety has paralleled the development of the science of microbiology and its extension into new and related areas such as tissue culture, recombinant DNA (rDNA) technology, and the use of animals in research and biotechnology. Work with infectious agents in the laboratory always includes risk. Since Robert Koch first isolated *Bacillus anthracis* in 1877,[19] the isolation and identification of an agent that causes a transmissible human disease, in many cases, has been followed by a laboratory-acquired infection (LAI) with that agent.

First LAI Studies

From an historical perspective, the epidemiological review of LAIs began slowly. Thirty years passed between the first reported case of typhoid fever in a laboratory worker and the first survey of LAIs. In 1915, Kisskalt sent a questionnaire to "numerous colleagues" in Europe and collected information on 50 cases (including 6 deaths) of laboratory-acquired typhoid fever dating back to 1885.[20] The mode of infection was known in 23 cases; in 16, mouth-pipetting was the cause. In 1929, Kisskalt reviewed 59 additional typhoid cases and 24 LAIs due to other infectious agents. Again, accidental ingestion through a pipette was the most common means of infection.[21] As a result of cases of typhoid among laboratory workers, papers recommending the use of mechanical pipetters to prevent LAIs appeared in the German scientific literature as early as 1907. A paper published by an Austrian physician in 1918 described 21 different mechanical devices for this purpose.[22]

The causative agent of brucellosis has long been recognized as a dangerous laboratory pathogen. In one episode during the winter of 1938–1939, 94 LAIs occurred, mostly among students in a three-story building, due to the generation of aerosols from a centrifugation operation. These infections were followed by a survey conducted by Meyer and Eddie in 1941.[23] They described 76 *Brucella* infections beginning in 1897, and 74 other LAIs in the United States between 1922 and 1939.

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[19] Koch R. The etiology of anthrax, based on the life history of *Bacillus anthracis*. *Beitr Biol Pflanz* 1877. 2: 277-308.
[20] Kisskalt K. Laboratoriumsinfektionen mit Typhusbazillen. *Z. Hyg. Infektionskr*. 1915. 80:145-162.
[21] Kisskalt K. Laboratoriumsinfektionen mit Typhusbazillen und anderen Bakterien. *Arch. Hyg. Bakteriol.* 1929.101:137-160.
[22] Reinhardt F. Prevention of Laboratory Infections. *Zentralblatt fur Bakteriologie und Parasitologie* 1918. 80(7):456-465.
[23] Meyer KF and Eddie B. Laboratory infections due to *Brucella*. *J. Infect. Dis.* 1941. 68:24-32.

The first U.S. Public Health Service-supported study on LAIs was conducted between 1949 and 1951 by Sulkin and Pike.[24] They surveyed 5,000 laboratories, of which half responded. It is interesting to note that only 35 percent of the 1,342 LAI cases captured in the survey had been acknowledged previously by inclusion in a publication. Although current regulations do not require that all LAIs be reported, failures to comply with mandatory LAI reporting, such as the reporting requirements in the *Select Agent Regulations*, still occur today.

A case of laboratory-acquired *Brucella* infection at Texas A&M University in February 2006[25] underscores the need for a national effort to improve the reporting of LAIs and other incidents with the potential to cause harm, and for an appropriate centralized mechanism through which to report them.

The Fort Detrick Experience

Many within the biosafety profession acknowledge Arnold G. Wedum as the "Father of Microbiological Safety." Wedum was the Director of Industrial Health and Safety Division at the U.S. Army Biological Research Laboratories at Fort Detrick, Maryland, from 1944 to 1969 and a leader in the development of the modern biocontainment facility. The Fort Detrick biological safety program was the largest of its kind, with 25 to 30 individuals on staff. The program was based on written safety policies and procedures that clearly delegated operational responsibilities, and described a comprehensive biosafety program that included adequately funded applied biosafety research.[26]

The Agent Control Branch of the Fort Detrick Industrial Health and Safety Division was organized into sections to support the six principal functions of the biological research laboratories: decontamination, pilot plant, aerobiology, animal facility engineering, research, and training. One of the program's many accomplishments was to establish and refine the concept of containment and the principles of biosafety used today. The safety principles included the use of primary barriers, facility controls (secondary barriers), and microbiological techniques (including many of the disinfection and decontamination methods used today). Other accomplishments of the Fort Detrick Industrial Health and Safety Division include the following:

- Demonstrated the effectiveness of spun fiberglass pads for filtering bacteria (1949)

- Specified and installed first Class I stainless steel biological safety cabinet (1950). Class III cabinets were installed in 1951

[24] Sulkin SE and Pike RM. Survey of laboratory acquired infections. *Am. J. Public Health* 1951. 41:769-781.
[25] Texas A&M failed to immediately report a 2006 case of laboratory-acquired *Brucella* infection as required under the *Select Agent Regulations*. Kaiser J. Biosafety Breaches: Accidents Spur a Closer Look at Risks at Biodefense Labs. *Science*. September 28, 2007. 317(5846):1852-1854.
[26] Wedum AG. Laboratory safety in research with infectious diseases. *Public Health Rep.* 1964. 79:619-33.

- Instituted the Biological Safety Conference, which started a strong collaborative tradition of professional development through sharing information about biosafety among colleagues who promoted safety in research and microbiology laboratories throughout the United States (1954). In 1984, the conference became the foundation and centerpiece for the American Biological Safety Association (ABSA). ABSA sponsored the 51st Biological Safety Conference in 2008; it continues the spirit of networking established in original conference meetings and now attracts international participation.

- Developed, tested and validated the concept of triple packaging for air transport of biohazards (1968-1969)

Development of Federal Biosafety/Biocontainment Requirements and Guidelines

The pioneering advances in biosafety and biocontainment at Fort Detrick provided the foundation for evaluating the risks of handling infectious microorganisms, for recognizing biological hazards, and for developing practices, equipment, and facility safeguards to control risk. Various Federal entities—USDA agencies (APHIS and ARS), and HHS agencies (CDC and NIH)—subsequently developed biosafety/biocontainment requirements and guidelines specific to their own missions and activities.

In 1974, CDC published a report entitled "Classification of Etiologic Agents on the Basis of Hazard." The report introduced the concept of establishing ascending levels of containment that correspond to the risks associated with handling infectious microorganisms with similar characteristics (e.g., mode of transmission). CDC grouped human pathogens into four classes according to their modes of transmission and the severity of disease they caused. A fifth class included non-indigenous animal pathogens whose entry into the United States was restricted by USDA policy.

Also in 1974, NIH published the "National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses." It included guidelines that established three levels of containment based on an assessment of the risk of transmitting cancer to laboratory workers from occupational exposures to animal oncogenic viruses, or to a suspected oncogenic virus isolated from a human. The guidelines did not describe methods for assessing risk to the community.

In 1976, NIH first published the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*), which described in detail the laboratory practices, equipment, and facility safeguards that correspond to four ascending levels of physical containment, and established criteria for assigning experiments to a containment level based on an assessment of potential hazards of the then-emerging recombinant DNA (rDNA) technology.

The *NIH Guidelines* were first developed as an outcome of a process by which scientists assumed responsibility for managing the risks of their own research activities by closely examining the potential hazards and necessary oversight of what was then a nascent and poorly understood technology. This process included a July 1974 report from the Committee on Recombinant DNA Molecules of the National Academy of Sciences that called for a voluntary moratorium on rDNA research, and the development of guidelines for the conduct and review of rDNA experiments. In February 1975, scientists convened the landmark Asilomar conference to examine the science and safety of rDNA technology. Participants at that event reaffirmed the value of developing guidelines. When published a year later, the *NIH Guidelines* embodied a scientifically based approach to the oversight of rDNA research. Since their origin, the *NIH Guidelines* have been revised frequently to reflect advances in science and the potential risks of working with rDNA agents.[27]

CDC and NIH then led a broad collaborative initiative involving scientists, laboratory directors, occupational physicians, epidemiologists, public health officials, and health and safety professionals that culminated in the development, in 1984, of the first edition of the *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*. The *BMBL* is a code of practice for biosafety and biocontainment in all microbiological and biomedical laboratories. It is now in its 5th edition,[28] which further expands the technical content by adding agent summary statements to describe a range of biological hazards, and recommends precautions and levels of containment appropriate for handling specific human and zoonotic pathogens in laboratories and other facilities that house laboratory vertebrate animals. Critical updates to the *BMBL* are published online.[29]

In 1985, a foreign quarantine regulation (42 CFR 71.54) was issued requiring a permit for the importation or distribution of etiologic agents, hosts, and vectors that could cause human disease. The rule has been updated several times since it was originally promulgated.[30]

Development of the Select Agent Regulations

[27] The current version of the *NIH Guidelines* is available at http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html.
[28] The fifth edition of the *BMBL* is available at http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm.
[29] Critical announcements and updates that have immediate public health, safety, or security interest are posted in the *Morbidity and Mortality Weekly Report (MMWR)* or on the CDC website. The *MMWR* is available at http://www.cdc.gov/mmwr/.
[30] The foreign quarantine regulations (42 CFR 71.54) promulgated on January 11, 1985, under the authority of the Public Health Service Act, as amended (42 U.S.C. 216, 243, 264 – 272), state that a person may not import into the United States, nor distribute after importation, any etiological agent or any arthropod or other animal host or vector of human disease, or any exotic living arthropod or other animal capable of being a host or vector of human disease unless accompanied by a permit issued by the Director, Centers for Disease Control and Prevention (CDC).

Congress passed Section 511 of the *Antiterrorism and Effective Death Penalty Act of 1996* due to heightened concern about the ease with which disease-causing agents could be obtained legally for illegal purposes. At that time, there were limited licensing, registration, or safety requirements for laboratories or individuals engaged in the transfer of disease-causing pathogens or toxins within the United States, and no Federal requirements to report the transfer of these agents. The passage of the 1996 legislation directed HHS to establish a list of biological agents and toxins with the potential to threaten public health and safety, develop procedures governing the transfer of those agents, and set training requirements for entities working with these "select agents." This legislation also introduced civil and criminal penalties and severe monetary fines for violations of the *Select Agent Regulations*.

The *Antiterrorism Act* of 1996 led to the establishment of the CDC Select Agent Program. Following the events of 2001, Congress significantly strengthened Federal oversight of the possession, use, or transfer of select agents with the passage of the *Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001* (*USA PATRIOT Act*) and the *Public Health Security and Bioterrorism Preparedness and Response Act of 2002* (*Bioterrorism Act*) and the *Agricultural Bioterrorism Protection Act* of 2002 (collectively, the Bioterrorism Acts). The *USA PATRIOT Act* provided that no "restricted person" could have access to select agents or toxins and listed the conditions that would identify a person as a restricted person.[31] The Bioterrorism Acts increased safeguards and security measures for select agents, strengthened the regulatory authorities of HHS, and granted comparable regulatory authorities to USDA over biological agents and toxins that pose a severe threat to animal health, plant health, animal products, or plant products. HHS delegated its authority to CDC, and USDA delegated its authority to APHIS.

CDC and APHIS implemented the Bioterrorism Acts through a series of regulations, which culminated with the publication of the final *Select Agent Regulations* (42 CFR 73, 7 CFR 331, 9 CFR Part 121) in the Federal Register on March 18, 2005.[32] The Select Agent Programs within APHIS and CDC have greatly enhanced oversight of the safety

[31] Under section 817 of the *USA PATRIOT Act* (18 U.S.C. 175b), a "restricted person' is identified as an individual who: (A) is under indictment for a crime punishable by imprisonment for a term exceeding 1 year; (B) has been convicted in any court of a crime punishable by imprisonment for a term exceeding 1 year; (C) is a fugitive from justice; (D) is an unlawful user of any controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802)); (E) is an alien illegally or unlawfully in the United States; (F) has been adjudicated as a mental defective or has been committed to any mental institution; (G) (i) is an alien (other than an alien lawfully admitted for permanent residence) who is a national of a country as to which the Secretary of State, pursuant to section 6(j) of the *Export Administration Act of 1979* (50 U.S.C. App. 2405(j)), section 620A of chapter 1 of part M of the Foreign Assistance Act of 1961 (22 U.S.C. 2371), or section 40(d) of chapter 3 of the *Arms Export Control Act* (22 U.S.C. 2780(d)), has made a determination (that remains in effect) that such country has repeatedly provided support for acts of international terrorism, or (ii) acts for or on behalf of, or operates subject to the direction or control of, a government or official of a country described in this subparagraph; (H) has been discharged from the Armed Services of the United States under dishonorable conditions; or (I) is a member of, acts for or on behalf of, or operates subject to the direction or control of, a terrorist organization as defined in section 212(a)(3)(B)(vi) of the *Immigration and Nationality Act* (8 U.S.C. 1182(a)(3)(B)(vi)).

[32] The *Select Agent Regulations* are available at http://www.selectagents.gov/selagentRegulation.htm.

and security of work with dangerous biological agents and toxins in the United States. The Select Agent Programs promote laboratory safety and security by enforcing the *Select Agent Regulations*, providing guidance to the regulated community, and inspecting facilities where work with select agents occurs.

Development of USDA Laboratory Safety Efforts[33]

For more than 100 years, the primary missions of USDA have been to protect U.S. agriculture and conduct research on all aspects of agriculture from farm to fork. The Bureau of Animal Industry (BAI) was established by Congress in 1884 to promote livestock disease research, enforce animal import regulations, and regulate the interstate movement of animals. Regulatory activities to protect U.S. crops began more than two decades later with the 1908 *Plant Quarantine Act* and the establishment of the Federal Horticultural Board to enforce the act. The Federal Horticultural Board was separated into various plant health bureaus in 1928.

In 1953, the functions of the BAI and the various plant health bureaus became part of USDA/ARS. Under the ARS structure, responsibility for plant and livestock health was located in either the ARS research or regulatory divisions, depending on the nature of the activity. In 1971, APHIS was established within USDA and given responsibility for regulatory and control programs relating to diseases and pests of animals and plants, which previously had been the responsibility of ARS.

APHIS entered the biotechnology era in 1985 when the Secretary of Agriculture designated APHIS as the agency responsible for regulating biotechnology-derived products that affect animal and plant health. This resulted in the establishment of the Biotechnology, Biologics, and Environmental Protection (BBEP) organizational unit within APHIS in October 1988. In 2002, BBEP became the Biotechnology Regulatory Services (BRS) program, a change that placed an increased emphasis on APHIS regulatory responsibilities regarding biotechnology. APHIS regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) through enforcement of the *Virus-Serum-Toxin Act*.[34] The Plant Protection and Quarantine (PPQ) division within APHIS,[35]safeguards agriculture and natural resources from the risks associated with the entry, establishment, or interstate movement of plant pests, biological control agents, prohibited plant material, and noxious weeds to ensure an abundant, high-quality, and varied food supply. In 2000, Congress rewrote and consolidated the various plant protection statutes under PPQ responsibility as the *Plant Protection Act, 2000* (*PPA*) (7 U.S.C. 7701 *et seq*.).

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[33] For more about the history of USDA/ARS, see http://www.ars.usda.gov/is/timeline/comp.htm. For more about the history of USDA/APHIS, see http://www.aphis.usda.gov/about_aphis/history.shtml.
[34] For a history of the *Virus-Serum-Toxin Act*, see http://www.nationalaglawcenter.org/assets/crs/RS22014.pdf.
[35] The broad regulatory authority APHIS/PPQ of is derived from the *Plant Quarantine Act*, 1918 and the *Federal Plant Pest Act*, as amended in 1957. These two acts were combined into the *Plant Protection Act*, 2000.

In 2002, Congress passed the *Animal Health Protection Act* (*AHPA*) (7 U.S.C. 8301 *et seq.* and related legislation). The *AHPA* consolidated all animal quarantine and related laws, some of which date to the late 1800s, and replaced them with one flexible statutory framework that better equips APHIS to perform its various roles in safeguarding animal health. The legislation provided APHIS with new authorities that enable it to provide an effective and efficient response to modern-day challenges that could threaten the health and safety of all aspects of U.S. animal agriculture, from farm to table. Although most of the authorities contained in the consolidated *AHPA* were taken from existing laws, some new provisions are a direct result of situations in which APHIS was unable to protect U.S. animal agriculture fully due to gaps in legal authority. For example, previous statutes did not cover the progeny of imported animals because of the belief that disease would be detected long before the imported animals were bred.

Important provisions of the *AHPA* and the *PPA* are the requirements for obtaining permits to transfer animals and plants from one location to another, and the inspection requirements for all areas of facilities in which work with regulated animal and plant pathogens, plant and animal products, or related regulated items occurs. Another important provision of the *AHPA* and the *PPA* strengthens the ability of APHIS to prosecute individuals who smuggle or move without an APHIS permit and inspection any animals, plants, animal or plant pathogens, plant products, animal products, or related regulated items into the United States. Under these statutes, severe civil penalties and significant monetary fines could be imposed or, if the action was a felony, criminal penalties could be imposed.

During the 1990s, ARS scientists and their counterparts in Australia's Commonwealth Scientific and Industrial Research Organization *(*CSIRO*)* noted that scientific exchanges were occurring sporadically among countries conducting research on foreign disease agents, with the common goals of protecting their respective livestock and poultry industries and ensuring and potentially expanding stable export markets. In October 1991, ARS and CSIRO co-sponsored a joint biosafety meeting in Knoxville, Tennessee, to focus on biocontainment issues and challenges associated with *in vivo* livestock research. Participants from Australia, Canada, England, The Netherlands, Spain, Switzerland, and the United States described the research missions, containment facilities, and policy and procedures of their respective institutions, and also discussed minimal common safety features. This meeting was the First International Veterinary Biosafety Workshop for Biosafety Officers, professionals who manage veterinary containment facilities for work with livestock species. The workshop also was the genesis of the International Veterinary Biosafety Working Group, an organization that published the *Veterinary Containment Facilities: Design and Construction Guide*[36] in 2006, and conducted its 12th international workshop in April 2008. ARS was the first agency to define BSL-3-Ag as a containment level and provide detailed information on the design and construction of these specialized animal facilities.[37]

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[36] The *Veterinary Containment Facilities: Design and Construction Guide* is available at http://tecrisk.com/projekte/projekt1/Handbook_070323.pdf.

[37] The ARS Manual 242.1, *ARS Facilities Design Standards*, chapter 9, contains detailed information on BSL-3-Ag containment, and is available at http://www.afm.ars.usda.gov/ppweb/PDF/242-01M.pdf.

International Standards for Biosafety Management

In addition to guidelines for laboratory safety developed by U.S. entities, the World Health Organization (WHO) *Laboratory Biosafety Manual*, third edition, published in 2004, describes guidelines for microbiological risk assessment, containment levels for human and animal pathogens, specifications for biological safety cabinets, laboratory techniques and safety practices, etc. The first edition of the WHO manual was published in 1983; since then, many countries have adopted its codes of practice for the safe handling of pathogenic agents.[38]

Another set of international standards for the management of biological risks in the laboratory resulted from a series of workshops held by the European Committee for Standardization (CEN)[39] in collaboration with WHO in 2007. The CEN publication that resulted, *Laboratory Biorisk Management Standard*, emphasizes a risk-management system approach.

Modern Biocontainment Laboratories and Definitions of Biosafety Levels

At today's modern high and maximum containment research laboratories, in which research on the most hazardous biological and agricultural agents and toxins occurs, laboratory personnel follow standard biocontainment and biosafety practices and procedures. These practices and procedures are designed to reduce the exposure of laboratory personnel, the public, agriculture, and the environment to potentially infectious agents and other biological hazards.

The overall objective of physical containment is to confine a hazardous organism or toxin, thereby reducing the potential for exposure to laboratory workers or persons outside the laboratory, and the likelihood of accidental release to the environment. Physical containment is achieved through the use of laboratory practices, containment equipment, personal protective equipment (PPE), and laboratory and facility design. Emphasis is placed on the primary means of physical containment, which include laboratory practices and the use of containment and PPE equipment within the laboratory. The basic practices and equipment are appropriate for protocols common to most research and clinical laboratories where work with human biohazards occurs.

The physical features of laboratory and facility design provide a secondary barrier to protect against the accidental release of organisms outside the laboratory or to the

[38] The World Health Organization (WHO) *Laboratory Biosafety Manual*, third edition, is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf.

[39] For more information about the European Committee for Standardization (Comité Européen de Normalisation or CEN), see www.cen.eu. The final version of the CEN publication, *Laboratory Biorisk Management Standard* (CWA 15793), is available at http://www.cen.eu/cenorm/sectors/technicalcommitteesworkshops/workshops/ws31.asp.

environment. Physical barriers to ensure containment are more elaborate in high and maximum containment facilities, which are designed for handling moderately to highly dangerous infectious agents and toxins. Although many of these protective measures are common across high and maximum containment laboratories, the criteria for containing human and agricultural agents vary in significant ways.

The use of specific containment equipment and procedures is determined through risk assessments conducted at individual research institutions. Important differences exist between risk-assessment criteria for public health and worker protection, and requirements for animal, plant, and agricultural containment. (See Chapter V for more information about how research institutions use risk-assessment procedures to determine the appropriate containment levels for work with biological hazards under specific laboratory protocols.)

Laboratory Containment for Human Pathogens

The *BMBL* delineates four ascending levels of containment for work with biological agents that are hazardous to humans. In this report, these biosafety levels (BSL) are referred as BSL-1, BSL-2, BSL-3 (high containment), and BSL-4 (maximum containment). Each level of containment is associated with specific laboratory practices, safety equipment, and facility safeguards. The *NIH Guidelines* similarly describe four levels of biocontainment (BL1 to BL4), which closely parallel those described in the *BMBL*.

BSL-1 is the basic level of protection and is appropriate for agents not known to cause disease in normal, healthy humans. BSL-2 is appropriate for handling moderate-risk agents that cause human disease of varying severity by ingestion or through percutaneous (through the skin) or mucous membrane exposure. BSL-3 is appropriate for agents with a known potential for aerosol transmission, for agents that can cause serious and potentially lethal infections, and for agents that are not indigenous or are otherwise exotic in origin. Agents that pose a high risk of life-threatening disease by infectious aerosols are restricted to maximum containment laboratories that meet BSL-4 standards. Various groups, including NIH, have issued standards for the design and construction of high containment facilities.[40]

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

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[40] For design and construction standards issued by the NIH Office of Research Facilities (ORF), which includes standards for BSL-3 and ABSL-3 facilities, see the 2008 *NIH Design Requirements Manual for Biomedical Laboratories and Animal Research Facilities (DRM)* (formerly called the *NIH Design Policy and Guidelines*), available at http://orf.od.nih.gov/PoliciesAndGuidelines/FacilitiesPoliciesandGuidelines/DesignRequirementsManualPDF.htm.

TABLE I
SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR INFECTIOUS AGENTS

BSL	AGENTS	PRACTICES	PRIMARY BARRIERS AND SAFETY EQUIPMENT	FACILITIES (SECONDARY BARRIERS)
1	Not known to consistently cause diseases in healthy adults	Standard Microbiological Practices	None required	Laboratory bench and sink required
2	• Agents associated with human disease • Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: • Class I or II BSCs* or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPE§: • Laboratory coats; gloves; face protection as needed	BSL-1 plus: • Autoclave available
3	• Indigenous or exotic agents with potential for aerosol transmission • Disease may have serious or lethal consequences	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of laboratory clothing before laundering • Baseline serum	Primary barriers: • Class I or II BSCs or other physical containment devices used for all open manipulation of agents PPE: • Protective laboratory clothing; gloves; respiratory protection as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhaust air not recirculated • Negative airflow into laboratory
4	• Dangerous/exotic agents which pose high risk of life-threatening disease • Aerosol-transmitted laboratory infections have occurred; or related agents with	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	Primary barriers: • All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body,	BSL-3 plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum, and decontamination systems

	unknown risk of transmission		air-supplied, positive pressure personnel suit	• Other requirements as outlined in *BMBL* text

[*] BSC – Biosafety Cabinet
[§] PPE – Personal Protective Equipment

Table 1 has been reprinted from the *BMBL*, fifth edition, Section IV.

Laboratory Containment for Animal, Plant, and Agricultural Pathogens

For work with certain hazardous agricultural agents involving research animals, the *BMBL* describes a combination of work practices and physical containment requirements used to reduce the risk of LAIs, exposure, and accidental release. As is the case for working with human biological hazards, the degree of protection recommended for work with plant, animal, and agricultural hazards is proportional to the risk associated with an agent and the proposed research operations.

Four biosafety levels are used for work with animal pathogens under specific laboratory protocols—ABSL-1, ABSL-2, ABSL-3, and ABSL-4.[41] For work with animal pathogens in a vivarium, the same four levels can be used, with an additional level called BSL-3-Ag[42] reserved for laboratory work with agricultural pathogens that affect food or food products. In addition, the USDA/ARS has issued technical criteria and standards for the design of its facilities.[43] Thus, combinations of laboratory practices, containment equipment, PPE, and special laboratory design can be combined to achieve different levels of physical containment and protection.

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

[41] As described in the *BMBL*, fifth edition, the animal containment levels considered equivalent to the high and maximum containment facilities for working with hazardous human pathogens and toxins are animal biosafety levels 3 and 4 (ABSL-3 and ABSL-4), and "enhanced" BSL-3 facilities.
[42] The *BMBL* describes BSL-3-Ag as "a special facility designed, constructed and operated at a unique containment for research involving certain biological agents in large animal species. BSL-3-Ag facilities are specifically designed to protect the environment by including almost all of the features ordinarily used for BSL-4 facilities as enhancements. All BSL-3Ag containment spaces must be designed, constructed and certified as primary containment barriers." Hazardous agricultural agents that could require BSL-3-Ag containment include foot-and-mouth-disease and highly pathogenic avian influenza virus (HP-H5N1).
[43] The USDA/ARS publication, *ARS Facilities Design Standards* (242.1-ARS) is available at http://www.afm.ars.usda.gov/ppweb/PDF/242-01M.pdf.

TABLE 2
SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR ACTIVITIES IN WHICH EXPERIMENTALLY OR NATURALLY INFECTED VERTBRATE ANIMALS ARE USED

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

[*] BSC – Biosafety Cabinet
[§] PPE – Personal Protective Equipment

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

In addition to the *BMBL* guidelines developed by NIH and CDC and facility standards developed by ARS, various entities (Federal and non-Federal) have developed regulations, requirements, and work practices for specific types of research with potentially hazardous agricultural agents.

- USDA/APHIS has developed regulations, internal facility parameters, and work practices for handling agents of agricultural significance. USDA requirements are unique to agriculture because of the need for protection against pathogens of economic or environmental impact and those that can affect international trade agreements. The fifth edition of the *BMBL* discusses for the first time enhancements beyond BSL-3 that may be required by USDA/APHIS for persons working in the laboratory or vivarium with certain veterinary agents of concern.

- The American Society of Tropical Medicine and Hygiene has published facility standards and practices for housing invertebrate vectors and hosts. Comparable to the biosafety levels described above, there are four Arthropod Containment Levels (ACL 1-4), each associated with standard or special practices, equipment (primary barriers), and facilities (secondary barriers).[44]

- Appendix G of the *NIH Guidelines* specifies physical containment levels for standard laboratory experiments and outlines practices, equipment, and facilities for Biosafety Level 1 (BL1) through Biosafety Level 4 (BL4). These containment levels closely parallel BSL-1 through BSL-4, as described in the *BMBL*.

- Appendix Q of the *NIH Guidelines* describes containment and confinement practices for research involving animals that are of a size or that have growth requirements that preclude containment under Appendix G of the *NIH Guidelines*. Experiments with animals that are subject to the *NIH Guidelines* include those in which the animal's genome has been altered by introducing rDNA into the germ line (transgenic animals), and experiments involving viable rDNA-microorganisms tested in animals.

- Appendix P of the *NIH Guidelines* addresses physical and biological containment for research involving plants containing rDNA, plant-associated recombinant microorganisms, and small animals that carry rDNA. The main goal of plant containment is to avoid the unintentional transmission of, or release of, either the genetic material of the recombinant plant, or microorganism or animal associated with a plant. Four biosafety levels— BL1-P, BL2-P, BL3-P, and BL4-P—outline physical and containment practices to provide flexible approaches to ensure the safe conduct of research.

[44] American Committee for Medical Entomology, American Society for Tropical Medicine and Hygiene. "Arthropod containment guidelines." A project of the American Committee for Medical Entomology and the American Society for Tropical Medicine and Hygiene. *Vector Borne Zoonotic Dis*. 2003. 3:61-98.

- Another set of guidelines for the biological containment of plants in a research greenhouse setting is *A Practical Guide to Containment: Greenhouse Research with Transgenic Plants and Microbes*, which includes containment recommendations for transgenic agents and pathogens.[45] The guide designates four biological containment levels for plants containing transgenic elements or infectious agents, called BL-1 through BL-4. The manual was produced by Information Systems for Biotechnology, a program at Virginia Polytechnic Institute and State University, and funded by a grant from USDA Cooperative State Research, Education, and Extension Service (CSREES).

- The U.S. Agency for International Development (USAID), Agricultural Biotechnology Support Project II (ABSP), and the Program for Biosafety Systems (PBS) published a fact sheet in 2004, entitled *Developing Biosafety Systems*. Rather than offering guidelines for laboratory safety practices, it summarizes major issues for consideration among countries that seek to develop a national biosafety system.[46]

Relationship between Biosafety and Biosecurity

In addition to guidelines for laboratory biosafety and biocontainment, the *BMBL* also provides information and guidance about laboratory biosecurity. The fifth edition of the *BMBL*[47] describes biosafety and biosecurity as "... related, but not identical, concepts. Biosafety programs reduce or eliminate exposure of individuals and the environment to potentially hazardous biological agents. Biosafety is achieved by implementing various degrees of laboratory control and containment, through laboratory design and access restrictions, personnel expertise and training, use of containment equipment, and safe methods of managing infectious materials in a laboratory setting."

The *BMBL* also describes biosecurity as it applies to work with biological hazards that affect human and animal health. "The objective of biosecurity is to prevent loss, theft, or misuse of microorganisms, biological materials, and research-related information. This is accomplished by limiting access to facilities, research materials and information. While the objectives are different, biosafety and biosecurity measures are usually complementary."

Several groups are examining the relationship between biosafety and biosecurity as described in current regulations and guidelines that pertain to research at high and maximum containment facilities. A recent article suggests that the definition of

[45] The "biological containment of plants" refers to the "use of biological means to block plant sexual and vegetative reproduction and to prevent the spread and persistence of genetic material in the environment." From: Traynor PL, Adair D, and Irwin R. *A Practical Guide to Containment: Greenhouse Research with Transgenic Plants and Microbes*. 2001.

[46] The U.S. Agency for International Development (USAID) brief, *Developing Biosafety Systems*, is available at http://www.america.gov/st/washfile-english/2004/June/20040617105128AKllennoCcM0.5659083.html.

[47] Quotation excerpted from *BMBL*, fifth edition, Section IV, "Principles of Laboratory Biosecurity."

biosecurity has expanded during the past few years and should be restricted.[48] "The concept of biosecurity should be limited to the prevention of the misuse of scientific activities for terrorist aims, in particular to keeping dangerous agents out of the wrong hands." However, in their recent report, the Commission on the Prevention of WMD Proliferation and Terrorism expresses a different view. "The currently separate concepts of biosafety and biosecurity should be combined into a unified conceptual framework of laboratory risk management."[49]

The issues of biosecurity and personnel reliability, although related to laboratory biosafety and biocontainment, are not the focus of this report but are being addressed by a Federal Working Group established by Executive Order 13486, *Strengthening Laboratory Biosecurity in the United States*. All three issues—biosafety/biocontainment, biosecurity, and personnel reliability—are important and are being explored in detail by the Federal Government.

Public and Congressional Concerns about the Oversight of BSL-3, BSL-4, and Equivalent Agricultural Containment Facilities

Media Coverage of Recent Lapses in Biosafety

High and maximum containment laboratories, designated as BSL-3, BSL-4, and equivalent agricultural containment facilities, include numerous administrative, procedural, and engineering controls, as well as facility design features (see Chapter III). Biosafety and biocontainment features notwithstanding, human error, accidents, and human exposures have occurred, have been widely publicized, and have understandably heightened public and congressional concerns about the safety of these facilities. Exacerbating public concern is that several of these incidents were not reported as required to the agencies responsible for oversight. Media coverage of recent lapses in biosafety and biocontainment fueled congressional inquiry.[50,51]

The GAO examined issues associated with the oversight of BSL-3 and BSL-4 laboratories in the United States. In October 2007, the GAO issued a preliminary report entitled *HIGH-CONTAINMENT BIOSAFETY LABORATORIES: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*.[52]

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[48] Zmorzynska A and Hunger I. "Restricting the role of biosecurity." *Bull Atomic Scientists*. 19 December 2008. Available at http://thebulletin.org/web-edition/features/restricting-the-role-of-biosecurity.
[49] *World at Risk: The Report of the Commission on the Prevention of WMD Proliferation and Terrorism*. Released December 2, 2008. Available at http://www.preventwmd.gov/report/.
[50] Margasak L. Dangerous Animal Virus on U.S. Mainland? *The Associated Press*, April 11, 2008 (http://www.newsvine.com/_news/2008/04/11/1423998-dangerous-animal-virus-on-us-mainland).
[51] Margasak L. New lab security report may signal need for pause. The Associated Press, October 16, 2008.
[52] The GAO preliminary report, HIGH-CONTAINMENT BIOSAFETY LABORATORIES: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States, is available at http://www.gao.gov/new.items/d08108t.pdf. HHS/CDC has provided corrections to the GAO preliminary report, but as of June 2009, the GAO had not issued a final, corrected report.

Congressional Hearing on Biosafety Oversight (October 4, 2007)

In response to public concerns and the GAO's preliminary report of 2007, the House Energy and Commerce Committee Subcommittee on Oversight and Investigations held a hearing on October 4, 2007, entitled, "Germs, Viruses, and Secrets: The Silent Proliferation of Bio-Research Laboratories in the United States."[53]

Chaired by Rep. Bart Stupak (D-MI), the hearing included witnesses from GAO, NIH, CDC, Texas A&M University, the Center for Biosecurity at the University of Pittsburgh Medical Center, the Center for Arms Control and Non-Proliferation, and the Sunshine Project. Two major questions were probed during the hearing:

- How many high-containment biosafety laboratories do we really need? Is it better to build new ones or expand existing facilities?

  The central issue in this discussion was the inability of any Federal agency to quantify the number of high-containment laboratories in the country. Underpinning that challenge is the lack of a uniform definition of "laboratory" or "facility," as well as the absence of any requirement to report the construction of facilities that are funded solely by private entities.

- Are biosafety laboratories really safe?

  The Subcommittee was not satisfied with the responses by those involved in the incidents at Texas A&M University and other institutions. Subcommittee members were concerned there is no Federal oversight involving agents requiring high containment that are neither select agents nor rDNA agents.

  In response, NIH and CDC officials testified that a new Trans-Federal Task Force on Optimizing Biosafety Oversight would be launched to undertake an in-depth analysis of the existing Federal biosafety/biocontainment oversight framework, identify any gaps in that framework, and present options and recommendations to the Secretaries of HHS and USDA for making it more seamless and effective.

[53] For testimony and information about the October 4, 2007, congressional hearing, see http://energycommerce.house.gov/index.php?option=com_content&task=view&id=105&Itemid=93.

III. CURRENT FRAMEWORK FOR FEDERAL, STATE, AND LOCAL BIOSAFETY AND BIOCONTAINMENT OVERSIGHT

Introduction

Laboratory biosafety and biocontainment are achieved through effective management programs within individual institutions where high and maximum containment research occurs (i.e., at the local level), in conjunction with oversight provided by Federal, State, Tribal, and municipal agencies. Institutions that possess and work with biohazards have a fundamental responsibility to ensure these materials are managed in a manner that controls risk. Risk management is achieved by technically proficient workers who understand the hazards associated with their activities, and who adhere to institutional policies designed to mitigate these risks. The importance of local review of biohazard risks and local responsibility for managing these risks is reflected in the various government regulations and guidance documents that have been promulgated to protect laboratory personnel, public health, agriculture, and the environment from exposure to biological hazards used in laboratories. Federal, State, and municipal oversight agencies have a responsibility to provide leadership, guidance, and regulatory direction to research institutions in the development and implementation of effective biosafety/biocontainment management programs.

Since their inception in the mid-20th century, biosafety and biocontainment principles have evolved to keep pace with the science of microbiology, as has the system of laboratory biosafety and biocontainment oversight (see Chapter II). This oversight system is embedded in policies, regulations, and guidelines designed to protect laboratory personnel, public health, agriculture, and the environment from accidental or deliberate exposure to hazardous biological and agricultural agents and toxins. The biosafety and biocontainment oversight framework recently has expanded, from a focus on laboratory practices and protective equipment, to a broader strategy that encompasses new and emerging risks associated with modern life sciences research. The biosafety and biocontainment oversight framework also has been modified to incorporate regulations and programs developed in response to an increased threat of bioterrorism and other crimes involving biological agents.

This chapter of the report by the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) describes the current biosafety oversight framework, including applicable Federal, State, and municipal guidelines and regulations, which function together with biosafety/biocontainment management systems at individual research institutions, i.e., at the local level, to provide a layered and redundant approach to minimizing risk from work with hazardous biological agents.

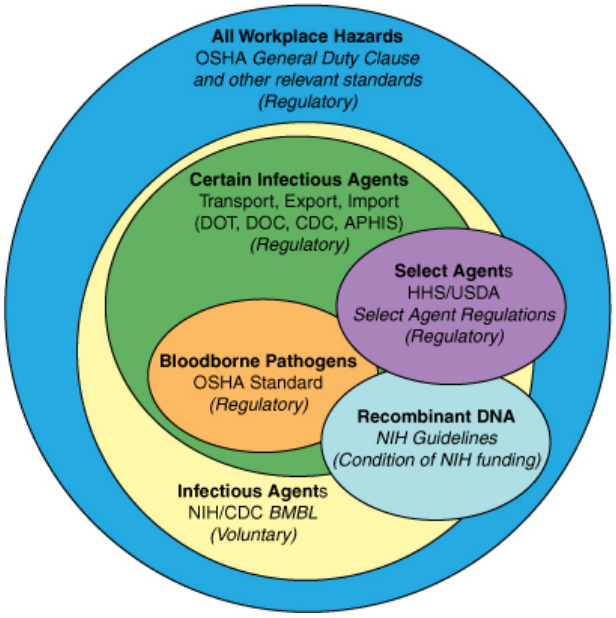
Multiple Levels of Biosafety and Biocontainment Oversight

Multiple, complementary, and sometimes overlapping biosafety and biocontainment oversight requirements exist within and among governments at the Federal, State, and municipal levels, as well as individual research institutions. Correspondingly, multiple government entities—at all levels—participate in the current system of biosafety and biocontainment oversight and, in many cases, coordinate their oversight activities with those of individual research institutions. The deliberate redundancy in the biosafety and biocontainment oversight framework helps ensure the protection of laboratory workers, public health, animals and plants, the food supply, and the environment from exposure to the hazardous agents and toxins used in laboratories. The individual elements of biosafety/biocontainment oversight vary, depending on the facilities and activities that require oversight, and the numerous agencies and institutions that play a role in a particular oversight activity.

How the Current System of Biosafety and Biocontainment Oversight Works: Federal Regulations and Enforcement Entities

Various Federal departments and agencies share responsibility for oversight of high and maximum containment research activities and facilities, depending on the nature of the research, as depicted in Figure 1. Certain Federal entities also are responsible for ensuring compliance with biosafety/biocontainment regulations, standards, and other requirements. (For a table showing the scope of Federal regulations, guidelines, and oversight entities, see Appendix C.)

Figure 1: Biosafety/ Biocontainment Regulations, Standards, and Guidelines Pertinent to High and Maximum Containment Research



The Federal regulations that pertain most directly to biosafety/biocontainment oversight at high and maximum containment research laboratories are the applicable Occupational Safety and Health Administration (OSHA) regulations (*General Duty Clause, Personal Protective Equipment Standards,* and *Bloodborne Pathogens Standard*); *Select Agent Regulations*, developed by the Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA); USDA Animal Plant Health Inspection Service (APHIS) permitting regulations; and HHS Centers for Disease Control and Prevention (CDC) regulations that require a permit for the import of any infectious agent known or suspected to cause disease in humans. Other Federal regulations and regulatory oversight, although ancillary to research on hazardous biological agents, can have an impact on high and maximum containment research facilities.[54] The Federal guidelines that pertain most directly to research activities in BSL-3, BSL-4, and equivalent containment facilities are the *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*), fifth edition, a guidance document developed by CDC and the National Institutes of Health (NIH), and the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*), which require compliance by any entity funded by NIH for recombinant DNA (rDNA) research. Other Federal agencies also require compliance with the *NIH Guidelines* as a term and condition of their own funding.[55]

Some of these regulations and guidelines focus on protecting humans from exposure to biological hazards; others are designed to ensure the effective containment of high-consequence agricultural agents that could endanger animal or plant health, or threaten the food supply; and some address both human and agricultural pathogens. OSHA regulations help ensure the safety of workers in all workplaces, including personnel in high and maximum containment research laboratories. The *BMBL* is designed specifically to protect laboratory workers from exposure to infectious organisms and certain biological toxins that pose various levels of risk to human health. Through its permitting system, APHIS regulates the transport and use of agents that are hazardous to agriculture (certain livestock, poultry, and crop pathogens); APHIS also inspects facilities to ensure they provide adequate containment of regulated agricultural agents. The HHS and USDA *Select Agent Regulations* cover both human and agricultural pathogens and toxins, and provide for Federal oversight of laboratories that possess, use, or transfer any agent or toxin on a designated list of select agents that pose significant risks to public health or agriculture. Various DOT, DOC, APHIS, and CDC regulations restrict the transfer (import, export, transportation within the United States) of hazardous biological agents unless certain conditions are met. The *NIH Guidelines*, which focus on work with rDNA, apply to high and maximum containment research on recombinant human and agricultural pathogens in addition to research that is performed under lower levels of containment.

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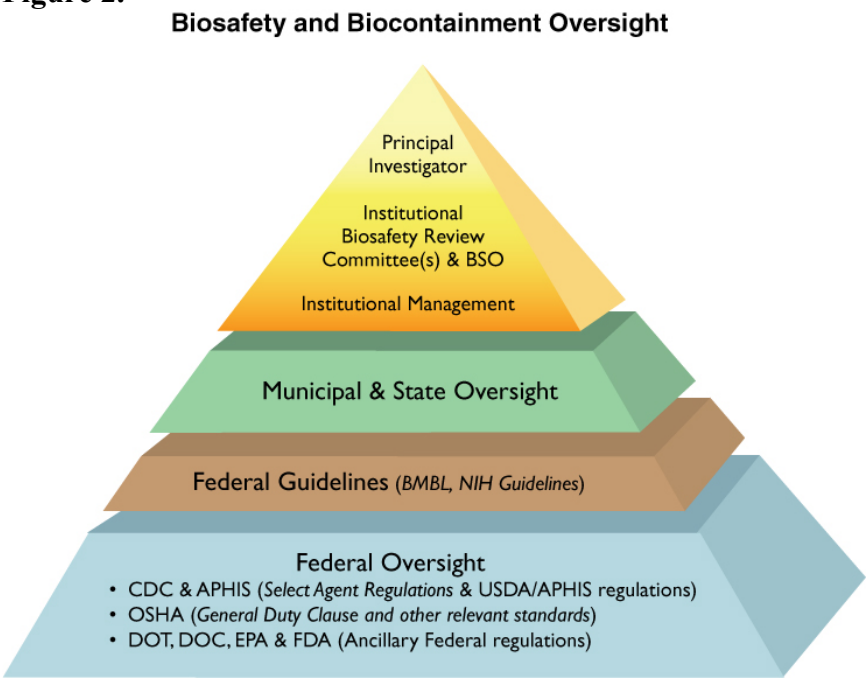
[54] The American Biological Safety Association (ABSA) has compiled a list of pertinent rules and regulations, which is available at http://www.absa.org/resrules.html.

[55] Compliance with the *NIH Guidelines* is required by the following Federal regulations: 7 CFR Part 340 *et seq*. (Introduction of "Organisms and Products Altered or Produced through Genetic Engineering which are Plant Pests or which there is Reason to Believe are Plant Pests").

The approach to biosafety and biocontainment oversight rests on a foundation of Federal regulations and guidelines, is provided at multiple levels, but is implemented locally, i.e., at individual research institutions, beginning with the principle investigators (PIs) who are responsible for the safety of activities in their laboratories. This pyramid of oversight is illustrated in Figure 2.

Figure 2.



OSHA Regulations and Standards to Ensure Workplace Safety

OSHA is responsible for the general oversight of workplace safety in the United States. OSHA regulations are based on the *Occupational Safety and Health Act of 1970* (*OSH Act*), 29 U.S.C. 651 *et seq*. OSHA has oversight authority for the safety and health of workers in all workplaces that fall under its jurisdiction, including individuals who work with hazardous biological agents or toxins in high and maximum containment research facilities. OSHA has jurisdiction over the safety and health of workers employed by private entities as well as all Federal Government (non-military) employees. (Section 19 of the 1970 *OSH Act*, 29 U.S.C. 668, contains special provisions to assure safe and healthful working conditions for Federal employees.[56])

In approximately half the States in the country, OSHA regulations also cover public employees (i.e., State, county, and municipal workers) through State-operated safety and health programs approved by Federal OSHA. These States, which are called State-Plan-

[56] For more information about OSHA regulations (Standards – 29 CFR), Part 1960, see http://www.osha.gov/pls/oshaweb/owastand.display_standard_group?p_toc_level=1&p_part_number=1960
.

States, are mandated to institute safety and health regulations that are at least as effective as those promulgated by Federal OSHA. In short, high and maximum containment research laboratories throughout the United States are expected to provide safe and healthful working conditions and must comply with the *OSH Act* and applicable OSHA regulations.[57]

- OSHA General Duty Clause (29 U.S.C. 654(a)(1)) Section 5(a)(1) of the *OSH Act* 29 U.S.C. 654, also known as the *General Duty Clause*, is an important provision that requires all employers to:

  > "…furnish to each of [its] employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to [its] employees."

  This provision allows OSHA to enforce workplace safety and health in all occupational settings covered by the *OSH Act*, particularly work environments in which OSHA does not have regulations addressing a specific occupational hazard. The *General Duty Clause* applies to all high and maximum containment research facilities that work with biological agents and toxins.

  If serious hazards are identified, the *General Duty Clause* requires that the employer implement feasible measures[58] such as engineering and work practice controls and the use of PPE to abate the hazard. Feasible abatement measures also may include hazards assessment, exposure monitoring, medical surveillance, and training.

  Federal guidance documents promulgated by the American National Standards Institute (ANSI)[59] and other industry groups have been adopted as OSHA requirements. Under the *General Duty Clause*, national consensus standards and best practices also can play a role in OSHA evaluations of whether employers have met their Section 5(a)(1) responsibilities. In cases involving the *General Duty Clause*, national consensus standards also can be evidence that an industry has recognized a specific or unique hazard and that there are feasible means to address it.[60]

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[57] "The *OSH Act* does not cover self-employed persons; farms which employ only immediate members of the farmer's family; working conditions for which other federal agencies, operating under the authority of other federal laws, regulate worker safety…: and employees of state and local governments, unless they are in one of the states operating an OSHA-approved state plan." Excerpted from DOL/OSHA compliance assistance available at http://www.dol.gov/Compliance/Guide/Osha.Htm#who.

[58] In this context, "feasible measures" refers to measures that can be achieved economically and technologically.

[59] For more information about ANSI, see http://www.ansi.org.

[60] Significance of ANSI standards with respect to OSHA requirements, specifically A92.6-1999. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=INTERPRETATIONS&p_id=24103.

Specific workplace regulations and standards promulgated by OSHA also pertain to high and maximum containment research facilities, and include the following:

- *Bloodborne Pathogens Standard* (29 CFR, 1910.1030). The OSHA *Bloodborne Pathogens Standard*, developed in 1991 and revised in 2001, mandates that employers protect workers from infection with human bloodborne pathogens in the workplace.[61] The standard requires that information and training must be provided before the employee begins work where occupational exposure to bloodborne pathogens may be present, annually thereafter, and before the employee is offered hepatitis B vaccination. This *Bloodborne Pathogens Standard* also requires advance information and training for all laboratory workers who work in HIV or HBV research laboratories. The standard was issued as a performance standard, meaning the employer also has a mandate to develop a written exposure control plan (ECP)[62] to provide a safe work environment, but is allowed some flexibility to accomplish this goal. Among other measures, the ECP requires employers to prepare an exposure determination, establish procedures for evaluating incidents, and determine a schedule for implementing the standard's requirements including engineering and work practice controls. The *Bloodborne Pathogens Standard* also requires employers to provide and pay for appropriate PPE for employees with occupational exposures. Although this standard applies only to human bloodborne pathogens, the protective measures in this standard (e.g., ECP, engineering and work practice controls, administrative controls, PPE, housekeeping, training, and post exposure medical follow-up) are the same measures for effectively controlling exposure to other biological agents and toxins.

- *Personal Protective Equipment Standards* (29 CFR 1910 subpart I). The OSHA *Personal Protective Equipment Standards* (*PPE Standards*) require that employers provide and pay for PPE and ensure that it is used wherever "hazards of processes or environment . . . [are] encountered in a manner capable of causing injury in the function of any part of the body through absorption, inhalation or physical contact" (29 CFR 1910.132(a)). In order to determine whether and what PPE is needed, the employer must assess the workplace to determine if hazards are present, or are likely to be present, which necessitate the use of [PPE]," 29 CFR 1910.132(d)(1). Based on that assessment, the employer must select appropriate PPE (e.g., protection for eyes, face head, and extremities; protective clothing; respiratory protection; and shields and barriers) that properly fits each affected employee (29 CFR 1910.132(d)(1)(iii)). The *PPE Standards* also include

[61] See also OSHA guidance on "Bloodborne Pathogens and Needlestick Prevention" available at http://www.osha.gov/SLTC/bloodbornepathogens/index.html. 29 CFR 1910.1030, *Bloodborne Pathogens Standard*, is available at http://www.gpoaccess.gov/cfr/index.html. Although the *Bloodborne Pathogens Standard* applies only to some research laboratories, its provisions provide a useful framework for nearly all laboratories described in this report.

[62] For a model Exposure Control Plan (ECP) developed by the National Institute for Occupational Safety and Health (NIOSH), see http://www.cdc.gov/niosh/docs/2007-158/. NIOSH, like OSHA, was created in 1970 by the Occupational Safety and Health Act; NIOSH is part of HHS/CDC whereas OSHA is part of DOL.

PPE specifications, which are drawn from national consensus standards. Employers must provide training for employees who are required to use PPE that addresses when and what PPE is necessary, how to wear and care for PPE properly, and the limitations of PPE (29 CFR 1910.132(f) and 1910.134(k)). The PPE standards include:

- Eye and face protection (29 CFR 1910.133)
- Respiratory protection (29 CFR 1910.134)
- Head protection (29 CFR 1910.135)
- Foot protection (29 CFR 1910.136)
- Hand protection (29 CFR 1910.138)

- Other OSHA standards. Additional OSHA standards pertain to high and maximum containment research facilities, or apply in certain situations (e.g., high and maximum containment research laboratories that use hazardous chemicals or human bloodborne pathogens, and emergency response operations involving the release of hazardous substances at these research facilities). The particular standards identified below are included because their provisions can help to eliminate or minimize exposure to biological agents and toxins and related accidents, injuries and illness; however, the following list is not exhaustive:

  - Occupational Exposure to Hazardous Chemicals in Laboratories (Laboratory Standard) (29 CFR 1910.1450)
  - Hazardous Waste Operations and Emergency Response (29 CFR 1910.120)
  - Sanitation (29 CFR 1910.141)
  - Medical Services and First Aid (29 CFR 1910.151)
  - Access to Employee Exposure and Medical Records (29 CFR 1910.1020)
  - Hazard Communication (29 CFR 1910.1200)
  - Retention of DOT Markings, Placards and Labels (29 CFR 1910.1201).

Failure to comply with applicable OSHA regulations and standards may result in the issuance of citations that carry monetary penalties for all serious workplace hazards. Several of the OSHA standards listed above require employers covered by the standard to perform hazard assessments of their workplaces to determine whether hazards are present (e.g., *PPE Standards* and *Bloodborne Pathogens Standard*). If hazards are identified, these standards also require covered employers, including high and maximum containment research laboratories, to institute measures (i.e., engineering controls, administrative controls, and work practices, as well as the use of PPE) to eliminate or minimize employees' exposure to workplace hazards, including in high and maximum containment research facilities that the standard covers.

The OSHA standards above also have various safety and health training requirements (e.g., *Bloodborne Pathogens Standard*, *PPE Standards, and Laboratory Standard*). Employee training is an important part of ensuring employee protection from injuries and illnesses. Many OSHA standards, including some of those listed above, mandate that employers train employees in the safety and health aspects of their jobs. Some of those OSHA standards require that safety and health training to be specific to the duties

assigned to employees, and to the safety and health hazards they could face (e.g., *Bloodborne Pathogens Standard, and Laboratory Standard*).[63] Laboratory employees, even those with extensive microbiological knowledge and experience, need safety and health training (e.g., training on the safe use of special equipment; understanding of site-specific safety rules and standard operating procedures, etc.) to assure they can perform job-related tasks at minimal risk to themselves, fellow employees, and the public. During inspections of certain biological containment facilities, OSHA has issued citations in cases where a facility's training records, employer or employee interviews, or other information revealed deficiencies in employee safety and health training, regardless of the education level of the employees involved.

- OSHA Inspections of Facilities. OSHA has no established National Emphasis Program (NEP)[64] or programmed inspection activity that specifies the random, periodic inspection of high and maximum containment research facilities across the country. However, as stated above, OSHA regulations do apply to these workplaces, and OSHA can and does perform inspections of these facilities to assure employee safety and health. OSHA's inspection presence in a broad range of research facilities has been largely in accordance with Standard Industrial Classification (SIC) codes 8731 and 8733[65] and is well documented in the agency's database. OSHA conducts inspections of these research facilities—few of which are high or maximum containment research laboratories—primarily in response to unprogrammed (unplanned) activities such as employee complaints, referrals from other agencies, reports of workplace accidents, etc.

[63] There is no OSHA standard that generally requires all high and maximum containment research facilities to train employees specific to the duties assigned and the hazards they face.

[64] National Emphasis Programs (NEPs) are enforcement strategies designed and implemented by the OSHA National Office. These programs are intended to address hazards or industries that pose a particular risk to workers. NEPs apply to all Federal OSHA Offices and in most situations; State Plan offices are encouraged to participate. NEPs are often accompanied by outreach to make employers aware of the programs as well as the hazards the NEPs are designed to reduce or eliminate.

[65] The OSHA Standard Industrial Classification (SIC) code "SIC 8731" refers to "Commercial Physical and Biological Research", and includes a wide range of commercial agricultural, biological, chemical, engineering, food, industrial, and physical research laboratories, as well as physical and biological commercial research and development (R&D) laboratories. There is no SIC code specific to high and maximum containment research laboratories. The code "SIC 8733" refers to non-commercial research organizations, including those for biological, economic, educational, medical, physical scientific, and sociological research, as well as for archaeological expeditions. There is no OSHA SIC code specifically for the high-containment biological and agricultural research facilities that are the purview of this Task Force. For more information about OSHA statistics and data, see http://www.osha.gov/oshstats/index.html.

From 1995 through 2007, there were approximately 1577 OSHA inspections conducted at research facilities in both Federal and State-Plan-States. Approximately 1143 of the 1577 inspections were unprogrammed. Of the total number of OSHA inspections conducted in this time period (1577), approximately 708 were conducted in response to employee complaints; 89 inspections resulted from workplace accidents. The sources of these accidents are not known; therefore it is difficult to determine how many, if any, of the accidents reported in this time frame involved exposure to hazardous biological agents. As a result of OSHA inspections for 1995−2007, the deficiencies most frequently documented by OSHA were for employers' failure to comply with the following OSHA standards:

- Laboratory Standard (29 CFR 1910.1450)
- Personal Protective Equipment (29 CFR 1910.132)
- Hazard Communication (29 CFR 1910.1200)
- Respiratory Protection (29 CFR 1910.134)

- OSHA and BLS Injury and Illness Data. Section 1904 of Title 29 of the Code of Federal Regulations, also called the "recordkeeping regulation," is the OSHA regulation that requires employers to record and report work-related fatalities, injuries, and illnesses. Most laboratories in research and clinical settings—including high and maximum containment research laboratories—are partially exempted from this regulation, however. Although these facilities are required to report to OSHA any workplace fatality or the hospitalization of three or more employees, other workplace injuries and illnesses are not routinely required to be recorded or reported unless the facilities are asked in writing to do so by OSHA, the Department of Labor Bureau of Labor Statistics (BLS), or a State agency operating under the authority of OSHA or the BLS. This partial exemption for research and clinical laboratories is extended to certain industries that OSHA has classified (based on particular SIC codes) as having low overall recordable work-related injuries and illnesses, in comparison to the national average for all industries. The BLS has estimated that research and development workplaces traditionally have a low incidence of recordable, work-related injuries.

  The BLS periodically requests a sample of employers in industries that have a partial recordkeeping exemption to record workplace injuries and illnesses for the following year in order to obtain information regarding those workplaces.[66] Pursuant to a BLS request for data about R&D facilities, BLS obtained injury and illness data for calendar year 2006. The 2006 sample survey not only included Category NAICS 5417 facilities involved in medical and biotechnology R&D facilities, but also those in which environmental, physical, agricultural, food, and electronic research is conducted. Consequently, the available injury and illness

[66] BLS now uses the North American Industry Classification System (NAICS) for categorizing certain industries. High and maximum containment research facilities that house biological hazards fall under the general category of scientific research and development (R&D) services, and are coded as NAICS 5417.

rates apply to a broad range of scientific R&D facilities from a sample survey of private industry settings.

The BLS sample survey for calendar year 2006 reveals a significantly lower rate of injuries and illnesses occurring among workers in scientific R&D facilities in comparison to the reported rates among workers in general industry. (A summary of sample survey data showing the numbers and rates of injuries and illnesses in scientific research facilities [NAICS 5417] for calendar year 2006 appears in Appendix D. The data do not include injury and illness rates from public or Federally operated facilities.)

HHS and USDA Select Agent Regulations

The possession, use, and transfer of select agents and toxins that have the potential to pose a severe threat to public health and safety, or animal and plant health and animal and plant products are regulated by HHS and USDA under the *Select Agent Regulations*, developed through close, interdepartmental collaboration.

Prior to the mid-1980s, there were no licensing requirements, registrations, or reporting requirements for entities that transferred certain human and zoonotic pathogens within the United States, other than the facility inspections and permits required by APHIS for regulated agricultural agents. In addition, there were no uniform safety or security requirements for entities that were performing these transfers. In 1985, a foreign quarantine regulation (42 CFR 71.54) was issued requiring a permit for the importation or distribution of etiologic agents, hosts, and vectors that could cause human disease.[67]

As a result of high-profile events involving the transfer of dangerous biological agents in the early 1990s, Congress passed Section 511 of the *Antiterrorism and Effective Death Penalty Act of 1996*, which directed the HHS Secretary to establish a list of biological agents and toxins that have the potential to pose a severe threat to public health and safety. The *Antiterrorism Act* also required the HHS Secretary to develop regulations establishing thorough procedures for the transfer of those agents to ensure that transfer entities have the appropriate training and skills to handle the agents safely, and the proper laboratory facilities to contain and dispose of those agents. The HHS Secretary delegated to CDC the responsibility for developing the Select Agent Program, and promulgating and implementing the new regulations.

In response to the events of 2001, Congress strengthened antiterrorism legislation. The *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*

[67] The foreign quarantine regulations (42 CFR 71.54) promulgated on January 11, 1985, under the authority of the *Public Health Service Act*, as amended (42 U.S.C. 216, 243, 264-272), state that a person may not import into the United States, nor distribute after importation, any etiological agent or any arthropod or other animal host or vector of human disease, or any exotic living arthropod or other animal capable of being a host or vector of human disease unless accompanied by a permit issued by the Director, Centers for Disease Control and Prevention (CDC).

authorized the regulation of the possession, use, and transfer of select agents and toxins. Title 2 of the 2002 *Bioterrorism Act*, specifically Subpart A, significantly expanded the regulatory authorities of HHS. Subpart B of the 2002 *Bioterrorism Act* (the *Agricultural Bioterrorism Protection Act of 2002*) (7 U.S.C. 8401) granted comparable regulatory authority to USDA for biological agents and toxins that present a severe threat to plant or animal health or products. The USDA Secretary delegated to APHIS the responsibility for promulgating and implementing the agricultural *Select Agent Regulations*.

The 2002 Bioterrorism Acts also required that USDA and HHS coordinate regulatory activities concerning those select agents and toxins that have the potential to cause a severe threat to public health and safety, as well as to agriculture. The Acts also require that HHS and USDA review the select agent list biannually to determine whether agents and toxins should be added or removed. Within 180 days of enactment of the 2002 Bioterrorism Acts, HHS/CDC and USDA/APHIS each published a set of *Interim Final Select Agent Regulations*, establishing a comprehensive set of regulations that included requirements for registration and security risk assessments. On March 18, 2005, CDC (42 CFR 73) and APHIS (7 CFR 331, 9 CFR 121) each published final regulations entitled "Possession, Use, and Transfer of Select Agents and Toxins."

The mission of the Federal Select Agent Program is to:

- Establish and enforce safety and security procedures for listed agents and toxins, including measures to ensure proper training and appropriate skills to handle agents and toxins, and proper laboratory facilities to contain and dispose of agents and toxins

- Establish and enforce safety and security measures to prevent access to listed agents and toxins for use in domestic or international terrorism or for any other criminal purposes

- Establish procedures to protect public health, animal and plant health, and animal and plant products, in the event of a transfer or potential transfer of a listed agent or toxin in violation of the safety procedures and safeguard and security measures established by the HHS or USDA Secretary

- Ensure appropriate availability of biological agents and toxins for research, education, and other legitimate purposes

The HHS/USDA *Select Agent Regulations* require registration for entities that possess, use, or transfer select agents or toxins. An entity applying to possess, use, or transfer a select agent must identify a single point of contact to represent that entity, the Responsible Official (RO), who must ensure compliance with the requirements of the *Select Agent Regulations*. The RO, and any other individuals within the entity who need access to select agents or toxins, must undergo a Security Risk Assessment (SRA) conducted by the Federal Bureau of Investigation (FBI), Criminal Justice and Information Services (CJIS), Division of the Department of Justice (DOJ).

All entities registered to possess, use, or transfer select agents or toxins must develop and implement a written security plan sufficient to safeguard the select agent or toxin from unauthorized access, theft, or loss. Entities also must develop and implement a written biosafety plan to safeguard against the release of select agents or toxins. The biosafety plan must be commensurate with the risk posed by the agent or toxin, given its intended use, and describe the biosafety and containment procedures for these agents and toxins. The *Select Agent Regulations* identify the *BMBL*, *NIH Guidelines,* and OSHA regulations in 29 CFR 1910.1200 and 1910.1450 as providing guidance for the establishment of safety provisions. Any entity that intends to conduct restricted experiments, as defined in the *Select Agent Regulations*, is required to receive approval from the Select Agent Program prior to conducting these types of experiments. All entities that possess, use, or transfer select agents or toxins also are required to:

- Develop and implement a written incident-response plan that must include response procedures for any hazards associated with the select agent or toxin

- Provide safety and security training for all individuals who work with or visit areas containing select agents and toxins that addresses the needs of the individual, the type of work the person will do, and the risks posed by the select agents or toxins

- Develop measures to ensure that select agents or toxins are transferred only to entities registered to possess the agent (transfers must be approved in advance by the Select Agent Program)

- Notify the Select Agent Program upon discovery of a theft, loss, or release of a select agent or toxin

- Maintain records associated with select agent or toxin possession for 3 years (e.g., inventory, access records, safety plans, transfer records, and training records)

Any entity possessing, using, or transferring select agents or toxins is subject to inspection prior to issuance of a Certificate of Registration to verify that the facility has accurately represented the information it has submitted to the Select Agent Program, and has in place the procedures and processes necessary to ensure compliance with the *Select Agent Regulations*. The *Select Agent Regulations* also permit unannounced inspections (42 CFR 73.18, 7 CFR 331.18, and 9 CFR 121.18). In addition to its inspection during the application process, every entity also is inspected during the Certificate of Registration renewal process. Additionally, inspections may be conducted when: 1) modifications are made to the entity's registration; 2) a new building or laboratory is added; 3) a higher-risk agent/toxin is added; 4) a change is made in security infrastructure or policy and procedures; 5) a theft, loss, or release incident occurs; and/or 6) a violation is reported. Since the publication of the *Select Agent Interim Final Rule* in 2003 (followed by the *Final Rule* in 2005), CDC and APHIS, in collaboration with their Federal partners, have conducted more than a thousand inspections of entities to ensure

that appropriate security and safety measures are in place to deter the theft, loss, or release of select agents and toxins.[68]

CDC and APHIS have released guidance to regulated entities to support compliance with the requirements of the *Select Agent Regulations*.[69] CDC, in conjunction with APHIS, has released guidance on complying with the security requirements and the theft, loss, or release reporting requirements of the *Select Agent Regulations*. These materials include informational documents on security and theft, loss, or release, inspection checklists, and training videos on the facility inspection process.[70] The Select Agent Program also provided a comprehensive, interactive course at the 2007 American Biological Safety Association (ABSA) meeting, which described the knowledge and tools necessary to develop biosafety plans, security plans, and drills and exercises to test incident-response plans.

HHS and USDA Regulations and Entities Governing the Import, Transfer, Transportation, and Use of Certain Biohazards

Several Federal departments and agencies regulate the transfer from one place to another and use of biological hazards and toxins that could endanger public health or agriculture. The regulations cover transportation of these materials within and to the United States (Department of Transportation [DOT] and USDA/APHIS), importation from other countries (HHS/CDC and USDA/APHIS), and export to other countries (Department of Commerce [DOC]). USDA/APHIS permits also specify facility and operational requirements for facilities that receive and will utilize agricultural pathogens. In addition, APHIS inspects facilities to ensure they are adequate for the containment of regulated agricultural agents.

- HHS/CDC: *Import Permit Regulations* (42 CFR 71.54). The CDC Etiologic Agent Import Permit Program (EAIPP) regulates the importation of etiological agents, hosts, and vectors of human disease (e.g., microorganisms and microbial toxins capable of causing disease in humans, bats, arthropods, snails, and non-human primate trophies) into the United States. The importation of etiologic agents is governed in part by section 71.54 (Etiologic agents, hosts, and vectors) of Title 42, Code of Federal Regulations, found in Part 71 (*Foreign Quarantine Regulations)*. When such materials are imported into the United States, they must be accompanied by a permit issued by the CDC Director. The EAIPP works in conjunction with the CDC Division of Global Migration and Quarantine (DGMQ),[71] which is charged with preventing the introduction, transmission, or

[68] Between 2003 and May 2009, CDC reported 820 inspections; APHIS reported 268.
[69] For more information about the Select Agent Program, see www.selectagents.gov.
[70] Also, representatives from the Select Agent Program hosted a workshop series entitled the "National Select Agent Program Workshop" in Riverdale, Maryland, for all registered entities and partners to inform individuals of their legal responsibilities for implementing the *Select Agent Regulations*. The next workshop series is scheduled for the summer of 2009 in Atlanta, Georgia.
[71] For more information about the HHS/CDC Division of Global Migration and Quarantine, see http://www.cdc.gov/nciDOD/dq/.

spread of communicable diseases from foreign countries into the United States, and the U.S. Customs and Border Protection (CBP) agency to ensure that all agents requiring an etiologic agent permit have been issued before importation into the United States. Any person violating any provision of 42 CFR Part 71 shall be subject to a fine or to imprisonment. For fiscal year 2008, the EAIPP processed approximately 2,000 permits to allow for the importation of etiologic agents, hosts, and vectors of human disease into the United States.

- USDA/APHIS Regulations. The regulatory authority of USDA/APHIS that affects importation and interstate transfer is provided in various acts passed by Congress, including the *Plant Protection Act* (7 U.S.C. 7701 *et seq*.), *Animal Health Protection Act* (7 U.S.C. 7701 *et seq*.), and *Virus-Serum-Toxin Act* (21 U.S.C. 151-159). These acts also provide the authority for APHIS to inspect facilities that possess or use plants, animals, or other biological agents and products (viruses, toxins, and sera) covered by the regulations. APHIS currently has 108 offices across the United States, and employs 116 personnel who conduct approximately 6,640 site inspections and process more than 13,000 permit applications each year.

  - USDA/APHIS: *Plant Protection Act* (7 U.S.C. 7701 *et seq*.). Under the authority of the *Plant Protection Act*, the USDA Secretary may prohibit or restrict the importation, entry, exportation, or movement in interstate commerce of any plant, plant product, biological control organism, noxious weed, article (including baggage, mail, garbage, earth, stone, and quarry products) or means of conveyance if such actions are necessary to prevent the introduction into or the dissemination within the United States of a plant pest or noxious weed. The USDA implementing regulations include 7 CFR 330 and 340.

  - USDA/APHIS: *Animal Health Protection Act* (*AHPA*) (7 U.S.C. 8301 *et seq*.) and related legislation. The *AHPA* consolidated all of the animal quarantine and related laws in existence, some dating back to the late 1800s, and replaced them with one flexible statutory framework that better equips APHIS to perform various functions to safeguard animal health. The *AHPA* authorizes the Secretary of Agriculture to prohibit or restrict the importation or movement in interstate commerce of any animal, article, or means of conveyance if the Secretary determines that the prohibition or restriction is necessary to prevent the introduction or dissemination of any pest or disease of livestock into or within the United States. Another important provision of *AHPA* has strengthened the ability of APHIS to prosecute individuals who smuggle any animals or animal products into the country, and assess a range of fines. The USDA/APHIS implementing regulations include 9 CFR 122.

  - USDA: *Viruses, Serums, Toxins, Antitoxins, and Analogous Products Act* (21 U.S.C. 151-159), also known as the *Virus-Serum-Toxin Act (VSTA)*. USDA is

authorized, under the 1913 *Virus-Serum-Toxin Act*, as amended by the 1985 *Food Security Act*, to ensure that all veterinary biologics produced in, or imported into, the United States are not worthless, contaminated, dangerous, or harmful. Federal law prohibits the shipment of veterinary biologics unless these are manufactured in compliance with regulations contained in Title 9 of the Code of Federal Regulations, Parts 101 to 118. Veterinary biologics for commercial use must be produced at a USDA-approved establishment, and be demonstrated to be pure, safe, potent, and efficacious.

Other Regulations Affecting High and Maximum Containment Research Facilities

Other regulations can affect specific high and maximum containment laboratories or specific tasks conducted by these types of laboratories (e.g., import, export, and transfer of hazardous agents (biological and non-biological); use of disinfectants, sterilants, or pesticides; certain R&D activities), but are ancillary to most research activities.

- DOT: Transportation of Etiologic Agents. The DOT[72] defines an "infectious agent" as a material known to contain or reasonably expected to contain a pathogen. A "pathogen" is a microorganism (including bacteria, viruses, rickettsiae, parasites, fungi) or other agent, such as a proteinaceous infectious particle (prion), which can cause disease in humans or animals (49 CFR 173.134(a)(1)). Infectious substances and the materials known or suspected to contain them are regulated as Division 6.2 (infectious) hazardous materials by DOT, under the Pipeline and Hazardous Materials Administration (PHMSA) *Hazardous Materials Regulations* (*HMR*; 49 CFR 171-180).[73] The *HMR* apply to any material DOT determines is capable of posing an unreasonable risk to health, safety, and property when transported in commerce. The packaging and shipment of an infectious substance must conform to all applicable *HMR* requirements when offered for transportation or transported by aircraft, motor vehicle, railcar, or vessel. For transport purposes, the term "infectious substance" is understood to include the term "etiologic agent."

  DOT regulations (49 CFR 172.802(a)(2) and (3)) also require that the shipping entity (e.g., Federal Express) must have a security plan that includes measures to address the assessed risk that might occur if unauthorized persons gain access to the hazardous biological material(s) being transported.

  The *HMR* for infectious substances are designed to prevent the release of these materials in transit to protect the public, workers, property, and the environment from the harmful effects that may occur from exposure to these materials. Protection is achieved through rigorous packaging requirements and hazard

[72] For more information about the responsibilities, enforcement authority, and compliance processes used by DOT and its 10 agencies, see http://www.dot.gov/.
[73] For more information about the Pipeline and Hazardous Materials Administration (PHMSA), an agency of DOT, see http://www.phmsa.dot.gov/home.

communication. Packages must be designed to withstand rough handling and other forces experienced in transportation, such as changes in air pressure and temperature, vibration, stacking, and moisture. Hazard communication includes shipping papers, labels, markings on the outside of packaging materials, and other information necessary to enable transport workers and emergency response personnel to identify correctly the material and respond efficiently in an emergency situation. In addition, shippers and carriers must be trained about these regulations so they can properly prepare shipments, and recognize and respond to the risks posed by these materials.

It is the task of the PHMSA inspection and enforcement staff to determine compliance with the *HMR* safety and training standards by inspecting entities that offer and transport hazardous materials for transportation; and that manufacture, requalify, rebuild, repair, recondition, or retest packaging (other than cargo tanks and tank cars) used to transport hazardous materials. The PHMSA hazardous materials enforcement program is prescribed in 49 CFR 107.301-339. There are civil penalties for inadvertent, non-willful violations, and higher penalties for willful violations of the *HMR* that lead to death or serious injury (49 CFR 107.333 and 107.335).

In addition to PHMSA's enforcement authority, the Secretary of Transportation delegates Federal enforcement authority for transporting hazardous materials to the Federal Motor Carrier Safety Administration (highway), Federal Railroad Administration (rail), Federal Aviation Administration (aircraft), and the Department of Homeland Security's United States Coast Guard (vessel). Each of these agencies has authority to enforce the *HMR*,[74] but emphasizes activities specific to their transportation mode or regulatory authority.

- DOC: *Export Administration Regulations* (15 CFR 730-774, including Chemical Weapons Convention requirements [15 CFR 745]) and the Commerce Control List (15 CFR 774 Supplement Number 1). The mission of the DOC Bureau of Industry and Security (BIS)[75] is to advance U.S. national security, foreign policy, and economic objectives by ensuring an effective export control and treaty compliance system and promoting continued U.S. strategic technology leadership.

[74] Sanctions authorized in the most recent transportation act (SAFETEA-LU; P.L. 109-59, August 10, 2005) but not yet incorporated into the *HMR* include enhanced authority to discover hidden shipments of hazardous material (49 U.S.C.A. 5103(b)(1) and 5121(c)); and the ability of PHMSA to issue or impose emergency restrictions without notice or an opportunity for a hearing, or prohibitions, recalls, or out-of-service orders only to the extent necessary to abate an imminent hazard (49 U.S.C.A. 5121(d)).

[75] The DOC Bureau of Industry and Security (BIS) implements and enforces *Export Administration Regulations* (*EAR*), which regulate the export and re-export of commodities, software, and technology, including biological commodities. Exporters may not export or re-export from the United States to certain countries and certain end-users biological commodities and technologies that are subject to the *EAR* without a license from BIS. In addition, BIS maintains a list of individuals and entities that either have a history of noncompliance with the *EAR* or for which compliance cannot be established. BIS also incorporates other U.S. Government agency lists into their end-user based controls, such as the Department of the Treasury Office of Foreign Assets Control "Specially Designated Nationals List." For more information about DOC/BIS, see http://www.bis.doc.gov/.

BIS accomplishes this mission, in part, by licensing exports of certain listed biological agents and toxins, and by assuring uniform application of DOC controls in international multilateral forums, such as the Australia Group,[76] and bilaterally with U.S. trading partners.

Under the authority of the *Export Administration Regulations*, BIS maintains a list of items (the *Commerce Control List* or "*CCL*") that includes biological agents and toxins, production equipment, delivery systems, and related technologies.[77] These items are derived from U.S. Biological Weapons Convention treaty obligations, U.S. commitments to the Australia Group, and unilateral foreign policy objectives. BIS also includes on its control list certain biological agents and toxins identified by other U.S. Government agencies (e.g., HHS/CDC and USDA/APHIS) as posing a severe threat to human, animal, and plant life. The inclusion of these export controls complements existing controls on possession, use, and transfer of these items within the United States.

- EPA Regulations Governing Antimicrobial Pesticides. The Environmental Protection Agency (EPA) regulates the sale, distribution, and use of antimicrobial pesticides under the authority of the *Federal Insecticide, Fungicide, and Rodenticide Act* (*FIFRA*) (7 U.S.C. 136-136y and 40 CFR 150-189).[78] Antimicrobial pesticides (e.g., sanitizers, disinfectants, and sterilants), which are used to decontaminate laboratories for a wide range of pathogens, are registered (licensed) by EPA in accordance with the requirements of *FIFRA*. Safety and efficacy-related data, as well as correct product labeling, are submitted to EPA as part of an application for registration. Before registering an antimicrobial pesticide, EPA must accept the data and labeling and conclude that the product will not cause "unreasonable adverse effects" when used in accordance with label directions and commonly recognized practices. This means that a registered antimicrobial pesticide product should be safe for humans and the environment and will be effective against its intended target when used properly. Finally, product users are required to follow all safety precautions and use directions on the labeling. Not following the label may be considered "use inconsistent with the labeling," which is a potential violation of *FIFRA*.

- FDA Regulations. The U.S. Food and Drug Administration (FDA) is responsible for the regulation of most types of foods, dietary supplements, drugs, vaccines,

[76] "The Australia Group (AG) is an informal forum of countries which, through the harmonisation of export controls, seeks to ensure that exports do not contribute to the development of chemical or biological weapons. Coordination of national export control measures assists Australia Group participants to fulfil their obligations under the Chemical Weapons Convention and the Biological and Toxin Weapons Convention to the fullest extent possible." For more information about the Australia Group, see http://www.australiagroup.net/en/index.html.

[77] For more information about the *Commerce Control List* (15 CFR Part 774, Supp. No. 1), see http://www.access.gpo.gov/bis/ear/ear_data.html.

[78] Information about the *Federal Insecticide, Fungicide, and Rodenticide Act* (*FIFRA*) and its enforcement is available at http://www.epa.gov/Compliance/civil/fifra/.

biological products, blood products, medical devices, radiation-emitting devices, veterinary products, and cosmetics.

- FDA *Federal Food, Drug, and Cosmetic Act*. Most Federal laws administered by the FDA are codified into the *Federal Food, Drug, and Cosmetic Act*,[79] which was amended in 2007. The act establishes safety and wholesomeness standards for food, safety standards for cosmetics, and safety and effectiveness standards for drugs, devices, and biological products. Other significant laws implemented by the FDA include the *Public Health Service Act*,[80] *Controlled Substances Act*,[81] and *Federal Anti-Tampering Act*.[82]

- FDA *Good Laboratory Practice (GLP) Regulations* (21 CFR 58). The FDA *GLP Regulations*[83] establish requirements for the conduct and reporting of nonclinical laboratory studies, and assure the quality and integrity of safety data. The *GLP Regulations* cover nonclinical research with biological products, food and color additives, animal food additives, human and animal drugs, devices for human use, and electronic products. FDA relies on documented adherence to GLP requirements in judging the acceptability of safety data submitted in support of research and/or marketing permits. FDA conducts inspections and data audits to monitor laboratory compliance with the GLP requirements.

- FDA *Current Good Manufacturing Practice (CGMP) Regulations*. FDA also has promulgated *CGMP Regulations*,[84] which govern the methods used in manufacturing, and the facilities and controls used for manufacturing. The FDA *CGMP Regulations* for drugs cover drug and biological product manufacturing and storage, among other things.[85]

Industry Standards Affecting Some High and Maximum Containment Laboratories

- Medical Laboratories—Requirements for Safety, ISO 15190, Geneva, International Organization for Standardization, 2003. The ISO standard (referred to as ISO 15190) provides the framework for management of a safety program as well as specific requirements for working safely in laboratories, including facilities in which workers handle infectious agents, chemicals, or radionuclides.

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[79] The 2007 version of the *Federal Food, Drug, and Cosmetic Act* is available at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.
[80] The *Public Health Service Act* is available at http://www.fda.gov/opacom/laws/phsvcact/phsvcact.htm.
[81] The *Controlled Substances Act* is available at http://www.fda.gov/opacom/laws/cntrlsub/cntlsba.htm.
[82] The *Federal Anti-Tampering Act* is available at http://www.fda.gov/opacom/laws/fedatact.htm.
[83] The FDA regulations "Good Laboratory Practice for Nonclinical Laboratory Studies" (21 CFR Part 58) are available at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=58.
[84] Information about the FDA *Current Good Manufacturing Practice (CGMP) Regulations* and proposed changes is available at http://www.fda.gov/cder/dmpq/.
[85] The FDA website with links to all FDA regulations related to Good Clinical Practices and Clinical Trials is available at http://www.fda.gov/oc/gcp/guidance.html.

Information about management of the laboratory safety program includes laboratory design, staffing, audits, reporting, training, safe laboratory practices, fire precautions, emergency evacuations, management of spills, waste management, and transport of specimens.[86]

- Protection of Laboratory Workers from Occupationally Acquired Infections, Clinical and Laboratory Standards Institute (CLSI), M29-3A; Approved Guideline, Third Edition. The CLSI document provides general safety guidance for clinical laboratories as well as functions and practices that can apply to other healthcare workplaces, and to research and animal facilities where exposures to infectious agents might occur. Additionally, specific guidance is provided for working with infectious agents of greatest concern to clinical laboratories (e.g., hepatitis B and C viruses, and HIV) and other infectious agents that can be transmitted by blood, aerosol, droplets, and body fluids. Aside from specific laboratory procedures to avoid exposures to infectious agents, other areas addressed include waste management, special precautions regarding procedures and equipment, and managing laboratory accidents.

Biosafety Guidelines and Requirements

Biosafety in Microbiological and Biomedical Laboratories (*BMBL*)

Over the past two decades, the *BMBL* has become the code of practice, authoritative reference, and *de facto* standard of operation for U.S. laboratory biosafety and biocontainment principles, practices, and procedures. The *BMBL*, first produced in 1984 and now in its fifth edition, is published jointly by CDC and NIH. Periodic updates to the *BMBL* are made to refine guidance based on new knowledge and experiences, and address new risks to laboratory workers and public health. Adhering to the *BMBL* is a requirement for entities in receipt of funding from DOD or HHS Public Health Service (PHS) agencies, including NIH, for certain classes of research grants and contracts, in accordance with 42 CFR 52.[87] The *Select Agent Regulations* cite the *BMBL* but do not require adherence to it,[88] although many Federal agencies require their own laboratory personnel to comply with the *BMBL* and recognize it as the minimal performance standard. Since its inception, the *BMBL* has served as a relevant, valuable, and authoritative code of practice at many biological research institutions.

The guidelines in the *BMBL* are designed to ensure the safety and security of working with biological agents, the protection of laboratory workers and the public, and the containment of biological hazards within the laboratory (thereby preventing their release

[86] See also Nobel MA. Medical laboratories – Requirements for safety. *JIFCC* 2004. 2003. 15 (4):1-3 available at http://www.ifcc.org/ejifcc/vol15no4/150412200405.pdf.
[87] 42 CFR Part 52 is available at http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title42/42cfr52_main_02.tpl.
[88] The *BMBL* is referred to in the *Select Agent Regulations* (42 CFR Part 73.12), and is used as the basis for safety inspection checklists in general biological laboratories.

into the environment). The *BMBL* emphasizes individual, site-, and procedure-specific risk assessment; the use of personal protective equipment, administrative and managerial controls; and facility safeguards to mitigate risk to laboratory workers, the public, and the environment. The *BMBL* encourages reporting of laboratory incidents through supervisory and agency-level chains of communication. It includes agent summary statements that provide information about biosafety requirements for infectious agents depending on the type of work being performed. The guidance in the *BMBL* applies to biomedical research laboratories and research animal facilities, although the general principles of biosafety and biocontainment apply to many other kinds of scientific facilities.

NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)

The *NIH Guidelines*[89] are the linchpin of the NIH system of biosafety oversight for entities it funds to work with rDNA. The *NIH Guidelines* specify scientifically based principles for the review and containment of organisms employed in rDNA research. They also articulate the responsibilities of institutions, investigators, Institutional Biosafety Committees (IBC),[90] Biological Safety Officers (BSO), the NIH Recombinant DNA Advisory Committee, and the NIH Director in the oversight of rDNA research.

The *NIH Guidelines* apply to any project involving rDNA[91] that is conducted at or sponsored by an entity that receives support for such research from NIH, or other agencies that require compliance with the *NIH Guidelines*. Even if a project is entirely privately funded, it is subject to the *NIH Guidelines* if the institution or the company where the work is being conducted has a grant or contract from NIH for conducting rDNA research. The logic for the broad applicability of the *NIH Guidelines* is that, to be effective, a biosafety program has to be observed by all researchers at a given facility.

The *NIH Guidelines* are termed "guidelines" because they offer principles and basic safety practices without being unduly prescriptive. The title of the document is not meant to convey, however, that the *NIH Guidelines* are optional. They are an important term and condition of receiving NIH funding for rDNA research in accordance with regulations governing grants for research projects (e.g., 42 CFR 52.8). An investigator or institution that disregards them is placing the institution at risk of special oversight or

[89] The *NIH Guidelines* are available at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.
[90] Institutional Biosafety Committee (IBC): An institutional committee created under the *NIH Guidelines* to review research involving recombinant DNA. The role of IBCs has evolved over time, and many committees also review other forms of research that entail biohazard risks as part of their institutionally assigned responsibilities. For more information about IBCs, see http://oba.od.nih.gov/rdna_ibc/ibc.html.
[91] NIH is proposing to broaden the scope of the *NIH Guidelines* to encompass work with nucleic acids (both DNA and RNA) that are synthesized chemically without the use of recombinant technology, and to address the biosafety principles and practices applicable to work with synthetic nucleic acids. This change reflects the fact that traditional rDNA techniques are no longer the only way to create new nucleic acid structures and that it is the use of the novel nucleic acid product—and not the technology used to create that product—that needs to be subject to biosafety oversight. The proposed changes will be published for public comment.

even a loss of eligibility for NIH funding. Several other Federal departments and agencies (e.g., Office of Naval Research; USDA APHIS, ARS, and the Cooperative State Research, Education and Extension Service [CSREES]; and Veterans Administration) have adopted the *NIH Guidelines* as a requirement for their intramural and extramural research programs.

The *NIH Guidelines* include two important components—the body and the appendices. The body of the document outlines administrative and review responsibilities that institutions assume when they receive NIH funds for rDNA research. The body also outlines the levels of institutional and Federal review that are necessary for various types of rDNA research. As the biosafety risk of the research increases, higher levels of review and approval are necessary. The appendices in the *NIH Guidelines* offer detailed guidance on such matters as risk levels of biological agents, the biosafety practices and containment measures applicable to the four biosafety levels, and the requirements for human gene transfer.

The *NIH Guidelines* require IBCs to have at least five members; collectively, the members must be qualified to review rDNA research. At least two of the five individuals who serve on an IBC must not be affiliated with the institution. These individuals allow for public participation in the review process, representation of community attitudes, and consideration of health and environmental concerns. When the institution is conducting rDNA research involving plants cultivated in greenhouses, or whole animals too large to use in normal laboratory conditions, the IBC must include an expert in plant or animal containment, respectively. A BSO must be appointed a member of the IBC if the institution is conducting rDNA research on a large scale (>10 liters) or in a high or maximum containment (biosafety level [BL]-3 or BSL-4; and BL3 or BL4) setting.

The *NIH Guidelines* require that institutions send to NIH all public comments made to them regarding the actions of their IBCs. This mechanism allows NIH to be aware of concerns regarding institutional biosafety practices and the biosafety aspects of the research underway at the institution. NIH responds as appropriate in keeping with the specifics of any public concerns.

State and Municipal Oversight of Biosafety and Biocontainment

State and municipal authorities are key stakeholders in efforts to ensure the principles of biosafety and biocontainment are implemented to protect laboratory personnel, the public, agriculture, and the environment from exposure to dangerous biological materials housed in biological research laboratories. The following discussion includes specific examples of State and municipal oversight systems for high and maximum containment facilities and their activities.

At the State level, a range of mechanisms ensures biosafety and biocontainment, including regulations to comply with environmental and occupational safety laws. State-specific requirements apply to many aspects of the operations of biological research

laboratories including, for example, the management of sharps and hazardous biological waste (e.g., the segregation, handling, labeling, storage, transport, and treatment of waste). In addition, biohazard waste generators and transporters, as well as storage and treatment facilities, are registered with the States and their operation requires a State-issued permit.

The *Public Health Security and Bioterrorism Preparedness Act of 2002* and related laws were intended to prevent select agents and toxins (as identified by 42 CFR 73.3 and 73.4, 9 CFR 121.3 and 121.4, and 7 CFR 331.3) from falling into the hands of terrorists by requiring Federal registration, inspection of laboratories that possess, use, and transfer select agents and toxins, as well as other security measures. State-specific regulations on the possession, use, and transfer of select agents and toxins often exist in addition to the Federal requirements applying to the same agents, but they vary among States with regard to their scope and requirements.

For example, the State of Maryland established the Biological Agent Registration (BAR) Program, which is managed by the Office of Laboratory Emergency Preparedness and Response at the Maryland Department of Health and Mental Hygiene. Annual State registration and periodic inspections are required for facilities working with select agents or high-consequence livestock pathogens and toxins, including genetically modified organisms or genetic elements encoding toxins, toxin subunits, or disease-associated factors from an organism listed as a select agent or overlap select agent. Maryland State law reporting requirements include the identification of biological agents and their location (laboratory and storage), containment/biosafety level, verification of receipt or transfer of biological agents, responsible officials' contact information, and a biological incident response plan.[92]

Similarly, laboratories working with infectious agents in the State of Connecticut need to register with the State Department of Public Health (biannual registration requires initial and periodic biosafety inspections by a State inspector). However, per the Connecticut Public Health Code (Regulation 19a-36-A25 to 19a-36-A35), reporting covers not only select agents but all agents capable of infecting humans (such as bacteria, viruses, parasites, fungi, and transmissible spongiform encephalopathies), their origin or source (animal), biosafety level, purpose of use, and information about the biosafety equipment and practices at the facility to be registered. Biosafety training (including refresher training) for the use of infectious biological agents in research is required as part of the Connecticut Department of Public Health registration for laboratories that use infectious agents; employee training records are made available to State inspectors during laboratory inspections.

In addition to Federal and State oversight of work with select agents, municipalities can elect to implement further or more stringent safety and accountability regulations. For

[92] For more information, see Maryland State law, Health-General Article, 17-601 *et seq*., Annotated Code of Maryland and the Code of Maryland Regulations 10.10.11 at http://www.dsd.state.md.us/comar/.

instance, the Boston Public Health Commission adopted *Biological Laboratory Regulations* that focus on high and maximum containment laboratories (BSL-3, BSL-4, and equivalent containment facilities) within the City of Boston area. These regulations, which became effective in December 2006, and associated *Guidelines for the Implementation and Enforcement of Boston Public Health Commission's Biological Laboratory Regulations*, require entities operating high or maximum containment research laboratories to apply for a permit and disclose their research activities. The regulations also mandate on-site inspections; ban any research that could enable weaponization of biological agents, and any classified or confidential research that cannot be disclosed to the Boston Public Health Commission; strengthen and expand the responsibilities of IBCs; and address incident-reporting, medical/occupational health surveillance, biological agent transportation, staff training, and effective on-site laboratory biosafety measures and security. In addition, the regulations establish a new authority, the Boston Biosafety Committee (BBC, composed of scientific and community representatives) to oversee the implementation and policies that govern high and maximum containment research laboratories, and require a community benefit program to address the impact of any new BSL-4 laboratory proposed for the community.

The city of Boston also has in place regulations regarding work with rDNA agents (as defined in the *NIH Guidelines*, 51 CFR 16958, May 7, 1986, as amended). The regulations require all institutions proposing any work with rDNA technology to obtain a permit before engaging in any activities, including permits for the construction or renovation of facilities where such work will be performed. The City of Boston also created a Boston rDNA Advisory Committee (BRAC), which is appointed by the City Commissioner to advise the Board of Health and Hospitals and the Commissioner about rDNA research regulations, production, and technology in the City of Boston. The 2006 City of Boston regulations establishing the BBC state that the BBC is to assume the responsibilities of the BRAC.[93]

Similar rDNA-related regulations are also in place for the City of Cambridge, Massachusetts, where the first municipal regulations on genetic research in the United States were implemented by a city ordinance in 1977. The ordinance was prompted by public debates about a Harvard University BSL-3 laboratory. The Cambridge Biosafety Committee, comprised of lay residents and administered by the Cambridge Public Health Department, oversees IBCs by reviewing their decisions and the records of their proceedings, and ensuring that the local community is represented. It also reviews new applications for permits or permit amendments if the work conditions or laboratory practices change.

Although the examples of State and municipal regulations mentioned above generally duplicate the Federal mandates, they also ensure that local authorities are more informed

[93] The 2006 City of Boston regulations establishing the Boston Biosafety Commission (BBC) are available at http://www.bphc.org/boardofhealth/regulations/Forms%20%20Documents/regs_LabRegFinal_9-19-06[1].pdf.

about the biological research taking place in their jurisdictions, which is a priority for establishing effective preparedness and emergency response plans. Engagement and coordination with local government authorities (including local public health officials) and the community via the emergency response plans mandated by the *Select Agent Regulations*, or via other means (i.e., public meetings of the IBCs), constitute an extra level of biosafety oversight for entities that operate biological research laboratories.

Biosafety Oversight at High and Maximum Containment Research Facilities

BSL-3, BSL-4, and equivalent containment agricultural research facilities all employ safety equipment, facility safeguards, and biosafety procedures and practices to prevent worker exposure to or the accidental release of hazardous agents or toxins. As indicated previously, biosafety principles, practices, and procedures are described in detail in the *BMBL*, and are widely utilized as the basis of good laboratory practice. Because biosafety oversight at the local (institutional) level is the foundation of an overarching system of oversight, it is important for all research facilities in all sectors to have in place personnel and mechanisms to assess the risks of working with the particular hazardous biological agents and toxins under study at the institution.

All personnel who work in high or maximum containment research facilities should be educated about the risks of handling hazardous agents and toxins because all play important roles in ensuring the biosafety of these laboratories. Some individuals, including the principal investigators (PIs) for particular research projects, bear increased responsibility. Others, known generally as biosafety professionals (BSOs and equivalents), play a critical role in managing an institution's biosafety program and have additional oversight responsibilities.

A combination of physical and procedural protective measures at high and maximum containment research facilities help ensure safety. All these institutions are required to comply with the regulations of various Federal agencies, depending on the nature of the institution's research activities and the hazardous agents under study. Although the scope of the Task Force report covers high and maximum containment research facilities (BSL-3, BSL-4, and equivalent agricultural facilities), it is important to note that lower-containment facilities also can be subject to Federal oversight, depending on the nature of their work.

Facilities at which research on hazardous pathogens and toxins occurs vary in their size, location, and research activities. Correspondingly, the equipment, design, and construction of these facilities are based on biosafety and biocontainment requirements and may vary according to the risks posed by working with certain biological agents or toxins. (See Tables 1 and 2 in Chapter II.)

Local Oversight Responsibilities and Mechanisms

At present, high and maximum containment research facilities have in place various biosafety professionals and mechanisms to provide biosafety oversight of their laboratories. For example, according to the *NIH Guidelines*, a research institution must establish an IBC to review research with rDNA if the institution receives NIH funding for rDNA research. However, many institutions that do not conduct rDNA research assign IBCs or similar committees broad responsibilities for assessing the risks of research involving infectious agents and other potential biohazards. The fifth edition of the *BMBL* (Section III, "Principles of Biosafety") indicates the need for an institutional body dedicated to biohazard risk: "Today, however, it is strongly suggested that an institution conducting research or otherwise working with pathogenic agents have a Biosafety Officer and a properly constituted and functioning IBC."

The responsibilities of IBCs with respect to oversight of research involving rDNA are described in the *NIH Guidelines*.[94] The responsibilities of other forms of institutional biosafety review committees, which often are modeled after IBCs, vary depending on the nature of research at the facility. The responsibilities of these review committees can include:

- Reviewing research conducted at or sponsored by the institution for compliance with relevant Federal regulations and guidelines. Such review requires different levels of evaluation at the institution(s) where the research occurs, depending on the nature of the work. For many low-risk experiments, investigators can simply notify the IBC at initiation of the experiment. Other experiments involve full IBC review and approval prior to initiation.

- Helping investigators determine the appropriate containment conditions in which to conduct their research. IBC recommendations are guided by one of several appendices in the *NIH Guidelines* that specify safety and containment practices for various forms of rDNA research.

- Assessing the adequacy of facilities, institutional procedures and practices, and investigator training and expertise for the type(s) of research being conducted

- Periodically reviewing research conducted at the institution to ensure compliance with relevant regulations and guidelines

- Adopting emergency plans covering accidental spills and personnel contamination resulting from research activities

- Reporting any significant problems with or violations of regulations and any significant research-related accidents or illnesses to the appropriate institutional official and relevant Federal entities

[94] Functions of IBCs are described in the *NIH Guidelines*, Section IV-B-2-b, and are available at http://www4.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm#_Toc7261584.

Today, many institutions have expanded the responsibilities assigned to IBCs or equivalent review committees beyond those described in the *NIH Guidelines*. Additional responsibilities often include the oversight of research involving potential biohazards other than rDNA, such as carcinogens (chemical and biological), infectious agents, and toxins. (See Chapter V, Objective 1, Recommendation 1.3, and Appendix E for additional information on local biosafety review committees [IBCs and equivalents]).

Biosafety Professionals

A BSO or equivalent biosafety professional plays a key role at many institutions where research with biohazards is conducted, particularly at high and maximum research containment facilities. A strong biosafety/biocontainment management program[95] at these facilities relies on the effectiveness of biosafety professionals who work with laboratory supervisors and/or principal investigators (PIs) to perform risk assessments prior to the initiation of research and when protocols or equipment change significantly. In many cases, biosafety professionals are part of a more comprehensive institutional health and safety program. These individuals typically are appointed by institutional management staff, and assume responsibilities for the day-to-day management of the institution's biosafety/biocontainment management program, which includes oversight of work with many different kinds of biohazards.

As with IBCs, the duties of BSOs are formally defined under the *NIH Guidelines*.[96] BSOs are responsible for the oversight of research with rDNA agents, and their presence is mandated for institutions conducting large-scale rDNA research or rDNA work in high (BSL-3) or maximum (BSL-4) containment laboratories.

The duties of BSOs and equivalent biosafety professionals vary, depending on the nature of the laboratory research, but can include:

- Conducting periodic inspections to ensure laboratory biosafety practices and procedures are rigorously followed

- Informing relevant authorities about the activities of the laboratory through routine reports, authorization requests, safety measures employed, inspections, etc.

- Reporting to the IBC (or equivalent biosafety review committee) and appropriate

[95] For a description of institutional biosafety/biocontainment management, also called laboratory biorisk management, see the standard (CWA 15793) developed by the European Committee for Standardization (Comité Européen de Normalisation or CEN), available at http://www.cen.eu/cenorm/sectors/technicalcommitteesworkshops/workshops/ws31.asp.

[96] Duties of BSOs are described in the *NIH Guidelines*, Section IV-B-3-c, and are available at http://www4.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm#_Toc7261585.

institutional official(s) any significant problems, violations of relevant regulations, and any significant research-related accidents or illnesses

- Interpreting and enforcing regulations and guidelines relevant to the safety, containment, and security of working with hazardous biological agents and toxins

- Providing technical advice to PIs and the IBC (or equivalent biosafety review committee) on research safety procedures

- Assessing the risk of occupational exposure and infection associated with handling hazardous biological agents and toxins, and communicating to laboratory workers the level of risk

- Serving as a resource for PIs and the IBC on risk management, e.g., determining appropriate level of containment for work with biological hazards

- Assisting in the development of emergency plans for handling accidental spills and personnel contamination, and investigating laboratory accidents

- Providing advice on laboratory security

Laboratory Supervisor and/or Principal Investigator

Individuals with primary and direct responsibility and liability for biosafety oversight are the PIs and other laboratory supervisors in individual laboratories. These individuals provide "front-line" supervision of laboratory activities and biosafety practices and procedures, and are directly responsible for the health and safety of their laboratory staff and visitors to their work area(s). A strong institutional biosafety/biocontainment management program relies heavily on PIs as well as on BSOs and members of IBCs who are knowledgeable about the risks of working with specific biological hazards, and who perform risk assessments prior to the initiation of research and when a protocol changes.

The PI or laboratory supervisor should be the individual who best understands the risks of working with particular hazardous biological or agricultural agents and toxins in their laboratory. These individuals typically are more experienced than other laboratory personnel and more familiar with the research protocols. In all laboratories, PIs or the laboratory supervisors are responsible for performing the initial risk assessments for work in their laboratories, and also for training laboratory workers to handle biological hazards. For this reason, PIs and laboratory supervisors must be knowledgeable about biosecurity issues, facility design, and the use of appropriate personal protective equipment, emergency response practices and procedures, and other aspects of laboratory safety and security that directly relate to the laboratory they manage.

Federal Efforts to Promote Biosafety Awareness

Federal departments and agencies with responsibility for biosafety oversight take steps to ensure that constituency groups and collaborators in the academic and private sectors are aware of biosafety regulations and guidelines, are informed about changes to regulations and guidelines, and understand the importance of complying with them. These efforts to promote biosafety awareness vary across Federal entities, but can include posting relevant biosafety information online, encouraging participation at conferences and meetings, and conducting outreach and distributing educational materials to program stakeholders. (A summary of biosafety outreach and educational activities by several Federal agencies appears in Appendix F.)

FOR AN OPTIMIZED FRAMEWORK OF BIOSAFETY AND BIOCONTAINMENT OVERSIGHT OF RESEARCH IN HIGH AND MAXIMUM CONTAINMENT FACILITIES

Introduction

The previous two chapters offer a brief history of biosafety and biocontainment practices and oversight, describe the importance of research that requires high and maximum containment, and explain the extensive biosafety and biocontainment oversight framework, with emphasis on oversight mechanisms used by individual research institutions and the Federal Government. These entities, together with oversight entities at the State and municipal levels, form a multilayered system of complementary and sometimes overlapping biosafety and biocontainment oversight measures.

Despite the multilayered and overlapping nature of the current biosafety and biocontainment oversight framework, the Federal Government recognizes that oversight of high and maximum containment research and related activities could be improved, and would benefit from a more formalized and systematic approach that includes uniformly applied standards. Currently, research with select agents, bloodborne pathogens, recombinant nucleic acids, and high-risk agricultural pathogens is subject to rigorous Federal and institutional oversight for most high and maximum containment research. Nevertheless, there are some gaps in the current oversight framework—not all potentially hazardous biological agents and not all research and related activities at high and maximum containment facilities are encompassed by existing Federal oversight mechanisms. Further, there is a need to ensure that biosafety and biocontainment oversight processes and procedures, personnel training, and relevant Federal regulations and guidelines are continually reviewed and strengthened.

This chapter is based on a comprehensive analysis by the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) of the current system of biosafety and biocontainment oversight of research and related activities at high and maximum containment facilities. Described below are (1) the vision and guiding principles for improving biosafety and biocontainment oversight; and (2) eight analysis-based objectives with corresponding issues, options, and recommendations for strengthening the current biosafety and biocontainment oversight framework.

Vision and Guiding Principles

Vision of the Task Force

The Task Force envisions that a national system for biosafety and biocontainment oversight of high and maximum containment research and related activities should achieve effective, comprehensive oversight at individual institutions where the research is conducted (local oversight), and by Federal agencies that conduct or support the research

(Federal oversight). Local and Federal oversight should be executed in a manner that protects laboratory personnel, public health, agriculture, and the environment while fostering the progress of research.

Guiding Principles

The guiding principles identified below apply to all aspects of the system for biosafety and biocontainment oversight of research and related activities at high and maximum containment facilities in all sectors (government [Federal, State, Tribal, and municipal], academia, privately funded research institutions, and private industry).

- Research on hazardous biological agents (pathogens and toxins) that requires high and maximum containment facilities is vital for ensuring public and agricultural health. The research contributes significantly to the understanding of human, plant, and animal pathogens and the diseases they cause; the development of new diagnostics, treatments, and preventive measures for protecting human, plant, and animal health; the development of a more robust and nutritious food supply; and the development of medical countermeasures for biodefense.

- Biosafety and biocontainment oversight must ensure the safe conduct of research without creating undue impediments to scientific progress. Rigorous adherence to biosafety and biocontainment standards and practices by all individuals and institutions involved in high and maximum containment research is essential to protecting laboratory personnel, public health, agriculture, and the environment. At the same time, it is critical that oversight measures allow important scientific research to proceed efficiently, and ensure sufficient flexibility so that new challenges to public health or agriculture, or emergency situations, can be responded to quickly and effectively.

- Local oversight is key to effective biosafety and biocontainment. The foundations of an effective and comprehensive system of biosafety and biocontainment oversight are the personnel, processes, and procedures in place at individual research institutions.

- Transparency and accountability are critical to the success of high and maximum containment research, as well as biosafety and biocontainment oversight of these research activities. Achieving transparency and accountability requires effective outreach and communication with the scientific community and the public.

- Periodic evaluations are essential to ensure effective oversight. There is a need for periodic and thorough evaluation of all components of laboratory biosafety and biocontainment oversight systems in place at all levels—from individual research institutions to the Federal Government—to ensure their effectiveness. The process of optimizing biosafety and biocontainment oversight must evolve as needs change.

Objectives for Improving the Current Biosafety and Biocontainment Oversight Framework

Ultimate Goal

The ultimate goal is to optimize biosafety and biocontainment oversight of research and related activities in high and maximum containment facilities in all sectors by developing a coordinated and synergistic approach that does not impede the scientific enterprise. Achieving this goal requires continual review and improvement of the biosafety/biocontainment framework as science advances and needs change. The Task Force has analyzed the current system of biosafety and biocontainment oversight, identified eight areas in which improvement is warranted, and defined eight objectives to address these areas. Presented with a discussion of each objective are specific issues, options, and the recommendations of the Task Force.

Acting on any of the objectives described below will require enhanced communication with and collaboration among Federal entities and their non-Federal partners. If the objectives are addressed effectively, the result should be enhanced biosafety/biocontainment management systems at high and maximum containment research facilities; an improved, multi-tiered system of biosafety and biocontainment oversight; and increased public confidence and trust that high and maximum containment research laboratories in the United States are being operated as safely as possible.

Summary of Objectives

1. Enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research through improved coordination of oversight activities.

2. Encourage a robust culture of accountability characterized by individual and institutional compliance with biosafety and biocontainment regulations, guidelines, standards, and policies.

3. Develop a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories.

4. Obtain and analyze information about laboratory incidents to enable trend analysis, minimize the number of future incidents, and share lessons learned, with the overall goals of optimizing laboratory safety and oversight.

5. Ensure that biosafety and biocontainment regulations and guidelines cover current and emerging hazardous biological agents, and develop an agricultural equivalent of the *BMBL*.

6. Ensure that the infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained.

7. Develop and support a national research agenda for applied biosafety and biocontainment to improve the management of biohazard risks.

8. Improve and share strategies to ensure effective public communication, outreach, and transparency about biosafety and biocontainment issues.

Issues, Options, and Recommendations for Improving the Current Biosafety and Biocontainment Oversight Framework

The Federal Government is committed to the highest possible standards for designing, constructing, maintaining, and managing high and maximum containment laboratories (BSL-3, BSL-4, and equivalent containment agricultural research facilities). It is also critical to optimize the training of personnel who work in and operate these facilities, in order to support the safe conduct of research activities that occur within them. With these fundamental needs in mind, the Task Force has developed a range of options and recommendations for strengthening the oversight of high and maximum containment research facilities in all sectors and improving their safety.

The Task Force developed its recommendations based on an analysis of objectives 1 through 8, and the associated issues and options. Suggestions offered at the public engagement meeting held December 8−9, 2008,[97] were also considered and included, as appropriate, in addition to recommendations derived from internal deliberations of the Task Force.

Each of the following chapters, Chapters V through XII, addresses one objective, with its corresponding issues, options, and recommendations. Chapter XIII then summarizes the objectives and recommendations. For some objectives, only one option is offered because the alternative option is to maintain the *status quo*. Implementing the recommendations of the Task Force will require additional resources from the Federal Government and/or individual research institutions. Many of the proposed recommendations identified by the Task Force could begin to be addressed immediately through existing organizational structures and mechanisms. Strategies for achieving objectives and implementing recommendations could be carried out, to the extent feasible, by Federal agencies using

[97] Information about the public engagement meeting held December 8−9, 2008, is available at https://www.hhs.gov/aspr/omsph/biosafetytaskforce/index.html.

their current authorities and current programs, and could be targeted to facilities over which they have authority. Implementing other recommendations, however, could require rulemaking or different legal mechanisms, and expanded or new regulatory and administrative entities. Many recommendations would require time to implement.

The recommendations that appear in Chapters V though XII are designed to apply to all high and maximum containment research laboratories in all sectors. In the short term, many recommendations propose requiring compliance and implementation by institutions that are Federally owned or funded by the Federal Government, and encourage compliance by individuals and institutions not receiving Federal funds. In the long term, the recommendations should lead to a culture of increased accountability by all relevant individuals and institutions, including those not owned or funded by the Federal Government. The Task Force recognizes that many of its recommendations may be relevant to entities outside the scope of this report, including BSL-3 and BSL-4 facilities used for non-research purposes, as well as BSL-1 and BSL-2 facilities and their agricultural equivalents.

These recommendations were developed without consideration of potential competing priorities across the Federal government, and their implementation would be subject to the availability of funds.

V. ENHANCED FRAMEWORK FOR BIOSAFETY AND BIOCONTAINMENT OVERSIGHT

OBJECTIVE 1: Enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research through improved coordination of oversight activities.

The Federal Government and individual high and maximum containment research institutions share responsibilities for the oversight of biosafety and biocontainment. An effective oversight framework must therefore coordinate activities at the Federal and local levels. Although the key elements, jurisdiction, and corresponding responsibilities for oversight vary for the Federal Government and local research institutions, both play critical roles in ensuring the safety of laboratory workers, public health, agriculture, and the environment. Vigilant and conscientious oversight of research and related activities at high and maximum containment facilities is critical to ensuring the accountability of relevant individuals and institutions, and to serving the needs and concerns of the scientific community and the public.

At the Institutional (Local) Level

As described in the *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*), effective biosafety and biocontainment oversight at individual research institutions is fundamental to the effectiveness and success of the overall framework for biosafety and biocontainment oversight. Therefore, an important goal for improving the current oversight framework is to ensure that all BSL-3, BSL-4, and equivalent agricultural biocontainment research facilities in all sectors have in place an effective biosafety/biocontainment management system. Risk assessment and risk management are the foundations of local oversight of high and maximum containment research activities. Both functions require that relevant personnel have sufficient scientific expertise and knowledge about biosafety and biocontainment standards and practices to be able to identify the most likely sources of risk to laboratory personnel, the public, agriculture, and the environment; and to identify the biosafety and biocontainment measures necessary to minimize those risks.

To function properly, an institutional biosafety/biocontainment management system and its associated personnel need the full support and collaboration of senior officials who manage the institution. Other components of this system also are critical:

- Clear, consistent, documented institution-specific policies and standard operating procedures to ensure safe work practices and effective containment within individual laboratories
- Access to a credentialed biosafety professional who is responsible for oversight of the institution's biosafety and biocontainment management program
- A local biosafety review committee that includes representatives from the community

- Thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment by an unbiased and appropriately constituted review body such as an institutional biosafety committee (IBC, as described in the *NIH Guidelines for Research Involving Recombinant DNA Molecules* [*NIH Guidelines*]) and appropriate risk-management methodologies
- Appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories
- Mechanisms for monitoring and evaluating the effectiveness of specific biosafety/biocontainment measures and institutional oversight mechanisms

Biosafety professionals. The goal is to have an adequately trained and credentialed biosafety professional(s) (e.g., a biosafety officer [BSO], which is discussed in the *NIH Guidelines*,[98] or equivalent professional) on site or accessible to all BSL-3, BSL-4, and equivalent biocontainment research facilities in all sectors. A strong, institutional biosafety/biocontainment management program relies on biosafety professionals who, together with laboratory supervisors and/or principal investigators (PIs), are knowledgeable about the risks of working with specific biological hazards, and who assist the PI or laboratory supervisor and biosafety review committee in performing risk assessments prior to the initiation of research and when protocols or equipment change significantly. Biosafety professionals must also be knowledgeable about the facility design, the use of appropriate personal protective equipment, emergency response practices and procedures, occupational health programs, and other aspects of laboratory safety. The biosafety professional(s) could assist senior institutional officials who manage high or maximum containment research facilities to help ensure that all laboratory and support personnel understand and comply with pertinent biosafety/biocontainment regulations and guidelines. The specific roles and responsibilities of institutional biosafety professionals would need to be formulated. (See Recommendation 1.3 and Appendix E.)

Local biosafety review committees and equivalents. A parallel goal to having a credentialed, appropriately trained biosafety professional is to ensure comprehensive review of all protocols utilizing biological hazards, including research conducted in high and maximum containment research facilities. This function may be accomplished by a biosafety review committee or its equivalent on which the biosafety professional serves. Local biosafety review may be accomplished by the IBCs described in the *NIH Guidelines* or committees modeled after IBCs, and may have responsibilities beyond those of IBCs.

Key features and activities of local biosafety review committees include: (1) experts who are knowledgeable about the high and maximum containment research activities conducted at the institution (to include representatives from the community); (2) the

[98] The *NIH Guidelines* require a BSO for review of BLS-3 and higher containment for protocols that will require work with recombinant DNA. If the work is not with recombinant DNA, a BSO is not required under the *NIH Guidelines*.

review of written protocols describing the research activities; and (3) authority to approve or disapprove a research protocol. In addition to the IBCs, which review protocols involving rDNA,[99] other examples of local (institutional) review committees include Institutional Animal Care and Use Committees (IACUCs), which help ensure the humane treatment of laboratory animals;[100] and the system of Institutional Review Boards (IRBs), which oversee human subjects research.[101] The specific roles and responsibilities, review procedures, and functions of local biosafety review committees or their equivalents would need to be formulated. (See Recommendation 1.4 and Appendix E.)

At the Federal Level

The current Federal biosafety/biocontainment oversight framework is multilayered and overlapping. Nearly all workplaces must comply with Federal regulations for ensuring workplace safety, and many high and maximum containment research facilities also must comply with Federal regulations designed specifically to protect the safety of laboratory workers, public health, agriculture, and the environment (for detail, see Chapter III). Nevertheless, the extensive framework now in place could benefit from improved coordination among all entities responsible for biosafety/biocontainment oversight of high and maximum containment research and related activities, including Federal agencies, State and municipal governments, and individual research institutions.

Issues, Options, and Recommendations to Address Objective 1

OBJECTIVE 1 − Issue 1.1: Although there are specific instances of coordinating biosafety and biocontainment oversight activities among Federal departments and agencies, there is no formalized or standardized mechanism to coordinate, as appropriate, all biosafety and biocontainment oversight activities across the Federal Government and with relevant non-Federal stakeholders.

To address this issue, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) considered identifying or establishing a Federal entity to coordinate biosafety and biocontainment oversight activities. Establishing a new Federal entity for coordinating oversight, or expanding the authority of an existing Federal oversight entity might require new legislative and/or regulatory authority depending on the role and activities of the entity. One option for structuring this coordinating Federal body could be to establish it in the White House Office of

[99] According to the *NIH Guidelines*, IBCs are required when an institution is performing non-exempt recombinant DNA experiments. For more information about the *NIH Guidelines*, see http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.

[100] For information about Institutional Animal Care and Use Committees (IACUCs), see http://www.iacuc.org/.

[101] For information about Institutional Review Boards (IRBs), see http://www.hhs.gov/ohrp/irb/irb_guidebook.htm.

Science and Technology Policy, and designate HHS and USDA as the lead agencies with participation by other relevant Federal agencies.

Considerations:

- Would provide a centralized mechanism for the Federal Government to coordinate biosafety and biocontainment oversight activities that affect all high and maximum containment research facilities in all sectors
- Could act as an information clearinghouse and resource to help improve collaboration and communication about biosafety and biocontainment practices and procedures, as well as shared oversight responsibilities
- Would help accomplish the objectives in this report by facilitating implementation of recommendations
- Might require new statutory and/or regulatory authority

The Task Force considered the option of not identifying or creating a centralized Federal entity to coordinate current biosafety and biocontainment oversight activities. However, given the importance of effective and comprehensive oversight at all levels of government and at individual research institutions, the Task Force recommends not maintaining the *status quo*. Such an approach could impede the pace of improving oversight of research and related activities at all high and maximum containment research facilities, and result in fewer improvements in the oversight framework.

RECOMMENDATION 1.1: Identify or establish a Federal entity to coordinate biosafety and biocontainment oversight activities, and to ensure comprehensive and effective Federal oversight for all high and maximum containment research facilities and activities in all sectors.

Rationale: Effective and comprehensive oversight of research and related activities at high and maximum containment research facilities is a shared responsibility of individual research institutions, State and municipal governments, and the Federal Government. Enhanced coordination of Federal biosafety and biocontainment oversight activities will facilitate the development and implementation of consistent regulations, policies, standards, and guidance documents that will strengthen biosafety and biocontainment practices at high and maximum containment research facilities. As proposed, the centralized, coordinating Federal entity would have access to the information and resources managed by its participating/supporting Federal departments and agencies, and would be able to acquire additional information, as needed.

Identifying or establishing a Federal entity for coordinating biosafety and biocontainment oversight activities would provide a centralized mechanism for the Federal Government to:

- Coordinate Federal oversight of biosafety/biocontainment research across the Federal Government and with non-Federal stakeholders, as necessary

- Coordinate development of a registry of all BSL-3, BSL-4, and equivalent containment facilities in the United States
- Evaluate the effectiveness of the Federal biosafety and biocontainment oversight framework on an ongoing basis
- Further enhance a culture of accountability and increase compliance with current biosafety and biocontainment regulations and guidelines, perhaps through the development of a mechanism for accrediting biosafety/biocontainment management programs at all high and maximum containment research laboratories in all sectors (Objective 2)
- Facilitate the development of a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories (Objective 3)
- Host and manage a centralized, voluntary, non-punitive, incident-reporting system that enables analysis of and information-sharing about incidents and lessons learned from all high and maximum containment research facilities in all sectors (Objective 4)
- Identify the need for and development of additional biosafety/biocontainment regulations, guidelines, or policies to ensure that all hazardous biological agents and institutions working with these agents are sufficiently covered by biosafety/biocontainment regulations, policies, and/or guidelines (Objective 5)
- Coordinate the development of mechanisms to ensure that infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained at all high and maximum containment research facilities (Objective 6)
- Guide and encourage the development of programs for applied biosafety and biocontainment research (Objective 7)
- Coordinate a broad array of communication mechanisms to (Objective 8 and others):
    - Identify and share best practices among high and maximum containment research institutions
    - Provide informational resources to high and maximum containment research institutions (e.g., about functional criteria that must be met when these facilities are being expanded or constructed)
    - Work with key stakeholders to develop clear standards for biosafety/biocontainment oversight, personnel training and competency, and incident-reporting; facilitate the development of improved training programs, etc.
    - Promote public communication, outreach, and transparency regarding biosafety and biocontainment oversight
    - Address congressional and public concerns about the safety and oversight of high and maximum containment research activities

Before identifying or establishing a new Federal entity, it will be important to engage representatives from relevant Federal agencies and non-Federal stakeholders (e.g.,

researchers, academicians, and representatives from private industry, State and municipal governments, and professional organizations) in determining its design and functions.

If a new Federal entity is created, or if an existing Federal entity expands its activities to take on the coordinating functions described above, it will be important to ensure that neither approach creates conflicts with existing responsibilities of the Federal departments and agencies currently responsible for biosafety and biocontainment oversight. Instead, the new Federal entity would have a coordinating role and facilitate robust interagency dialogues toward the development of scientifically sound and comprehensive biosafety/biocontainment policies rather than create an additional layer of Federal oversight.

Short-term steps:

- Determine the priority areas of biosafety and biocontainment oversight that would benefit from increased coordination by a single Federal entity
- Review biosafety and biocontainment oversight systems developed by other countries or international entities for ideas and lessons learned
- Review information about different kinds of oversight systems in a range of U.S. Federal agencies, and consider the current efforts to improve biosafety, biosecurity, and personnel reliability
- Identify whether an existing Federal entity could assume these responsibilities, or whether a new entity would need to be created

Long-term steps:

- If a new entity is deemed necessary, determine:
  - What legal mechanism(s) would be needed for its establishment
  - How such a new entity would interact with the Federal oversight entities that already exist (e.g., the HHS/USDA Select Agent Program, USDA/APHIS permitting system, etc.)
  - What its functions would be and how they would be achieved
- How to establish, staff, and sustain the new entity and ensure it functions effectively

OBJECTIVE 1 − Issue 1.2: Although Federal agencies track the high and maximum containment facilities for which they have regulatory oversight and can identify facilities they fund, the Federal Government currently has no centralized resource for identifying and tracking all high and maximum containment facilities in the United States.

To address this issue, the Task Force considered developing a registry of all high and maximum containment research facilities in the United States. Such a registry would support the new Federal entity in its efforts to ensure comprehensive, coordinated Federal biosafety and biocontainment oversight for these facilities. It also would address concerns raised in the 2007 GAO preliminary report, *HIGH-CONTAINMENT BIOSAFETY LABORATORIES: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*, and the 2008 Weapons of Mass Destruction (WMD) Commission report, *World At Risk*. These reports

criticized the lack of a single Federal agency or entity responsible for maintaining information on—or oversight for—all high and maximum containment facilities in the United States.

Considerations:

- Would provide a centralized registry for the Federal Government to identify and track all high and maximum containment research facilities in all sectors[102]
- Would provide a tool to assist the Federal Government in assessing whether the number of high and maximum containment research facilities in the United States is appropriate in relation to current knowledge gaps and research needs for work conducted at such facilities
- Would help the Federal Government ensure that effective and comprehensive biosafety and biocontainment oversight occurs at all high and maximum containment research facilities in all sectors
- Would enable further transparency and information-sharing related to current and future high and maximum containment research activities in the United States
- Establishing a comprehensive registry and requiring all BSL-3, BSL-4, and equivalent agricultural facilities to register might require new statutory or regulatory authority

The Task Force considered the option of not developing a registry of all high and maximum containment facilities in the United States. However, given the benefits associated with establishing and maintaining a comprehensive, centralized registry of these facilities, the Task Force recommends not maintaining the *status quo*. Such an approach would unnecessarily limit the Federal Government's efforts to enhance the current oversight framework and ensure that comprehensive and effective oversight mechanisms are in place for all high and maximum containment research facilities in all sectors.

RECOMMENDATION 1.2: Develop a registry of all high and maximum containment research facilities in the United States.

Rationale: A comprehensive and up-to-date registry of all high and maximum containment research facilities in the United States is essential to enhancing the current oversight framework for these facilities. The 2007 GAO preliminary report on BSL-3 and BSL-4 laboratories states that "no single [F]ederal agency has the mission and, therefore, is accountable for tracking the number of all BSL-3 and BSL-4 labs within the United

[102] Currently, all maximum containment laboratories in the United States are registered with the HHS and USDA Select Agent Program because all BSL-4 and equivalent agricultural facilities possess, use, or transfer select agents. However, not all high containment laboratories are registered with these or other agencies. The comprehensive registry that is envisioned would include high and maximum containment research facilities already registered, as well as those not captured by the current system.

States…."[103] The GAO report also indicates that no Federal agency is responsible for determining the risk associated with expanding the number of high and maximum containment laboratories. The development of a centralized registry also would support the 2008 WMD Commission report recommendation that the Federal Government "…consider centralizing the regulatory functions for biosafety and biosecurity by developing a new oversight mechanism for high-containment laboratories…."

A centralized registry, if developed, would allow the Federal Government to account for all high containment laboratories, including those not currently registered for work with select agents, and could be a useful tool in assessing whether the number of high and maximum containment research facilities in the United States is appropriate, given current knowledge gaps and research needs for work conducted at such facilities. Information gleaned from a registry would be useful for implementing some of the proposed communications regarding appropriate biosafety and biocontainment measures. A registry also would enhance awareness of and facilitate oversight of high and maximum containment research facilities that currently are not subject to Federal regulation. Further, a registry of all high and maximum containment research facilities could help enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research by facilitating coordination of oversight activities.

Short-term steps:

- Establish definitions of and parameters for BSL-3, BSL-4, and equivalent agricultural containment facilities to be covered by the registry
- Identify and review existing sources of information on the number and locations of high and maximum containment facilities in the United States, and develop approaches for integrating and maintaining information from these sources
- Identify types and categories of high and maximum containment research facilities that are not captured under current regulatory oversight mechanisms or reporting requirements
- Through consultation across relevant Federal agencies, establish processes for information-sharing and for protecting against unauthorized access to or inadvertent release of registry information
- Determine whether an existing Federal entity or a new entity should assume primary responsibility for developing, implementing, and managing the centralized registry

Long-term steps:

- Define the specific characteristics of the centralized registry and the processes required for its development, implementation, and maintenance
- Compile and integrate information from existing sources about the number and locations of high and maximum containment facilities

[103] The WMD Commission report make a similar point (p. 29): "…many BSL-3 laboratories that work with dangerous but unlisted pathogens, such as the SARS virus, operate outside of federal regulation and indeed even federal knowledge of their existence."

- Conduct outreach to the research community and other relevant stakeholders regarding requirements and processes for registration of facilities
- Implement processes for obtaining information about high and maximum containment research facilities already registered, and on facilities not currently captured by existing mechanisms
- Develop processes for keeping the proposed registry up to date, i.e., obtaining reference information on new high and maximum containment research facilities and changes in the status of existing facilities
- Maintain the centralized registry and ensure that it functions effectively

OBJECTIVE 1 − Issue 1.3: Many institutions where high or maximum containment research is conducted have a credentialed (certified or registered) biosafety professional (BSO or equivalent) who is responsible for managing biosafety and biocontainment oversight, although there is no universal requirement for this individual at the local (institutional) level. In addition, there is no requirement for all institutions with high and maximum containment research facilities to designate a senior institutional official with the appropriate knowledge, expertise, and authority who is responsible for ensuring institutional compliance with Federal biosafety/biocontainment regulations and guidelines.[104] In other arenas of research oversight, such as research with humans, animals, and select agents, a senior institutional official provides formal assurance that the institution is complying with pertinent Federal requirements.

To address this issue, the Task Force considered the option of requiring all institutions in all sectors with high or maximum containment research facilities designate 1) a senior official with the appropriate expertise and authority who is responsible for ensuring institutional compliance with Federal biosafety/biocontainment regulations and guidelines, and 2) a credentialed biosafety professional who is responsible for oversight of biosafety and biocontainment programs.

Considerations:

- Would help clarify responsibility within individual institutions with high or maximum containment research laboratories, and enhance the consistency of institutional oversight practices
- Would provide an assurance that the institution is complying with pertinent Federal requirements
- Would provide critical links among laboratory personnel, institutional biosafety professional(s), biosafety review committee(s), and upper-level management
- Would help promote public confidence and trust that institutional oversight is consistent and effective

[104] An individual who is responsible for ensuring institutional compliance with Federal biosafety/biocontainment regulations and guidelines also could be tasked with ensuring compliance with relevant State and/or municipal biosafety/biocontainment requirements.

- May not have the appropriate or adequate expertise (i.e., a credentialed biosafety professional and a senior institutional official) at some institutions (see Recommendation 3.3)

The Task Force considered the possibility of not recommending that all high and maximum containment research facilities designate a senior official and a credentialed biosafety professional with the responsibilities just described. This option, in effect maintaining the *status quo*, would fail to realize an essential component of local oversight—i.e., ensuring that all institutions with a BSL-3, BSL-4, or equivalent agricultural containment facility have individuals with the requisite expertise and authority to ensure that biosafety and biocontainment oversight is internally consistent and effective. Given the consensus of the Task Force that the most important level of biosafety and biocontainment oversight occurs within individual research institutions, these two individuals are fundamental to the effectiveness of the overall biosafety and biocontainment oversight framework.

RECOMMENDATION 1.3: Require that all institutions conducting high and maximum containment research designate: (1) a senior official with the appropriate knowledge, authority, and accountability who is responsible for institutional compliance with biosafety and biocontainment regulations and guidelines; and (2) a credentialed biosafety professional (see Recommendation 3.3) who is responsible for oversight of biosafety and biocontainment programs.

Rationale: There must be a strong level of commitment to biosafety and biocontainment oversight at all institutions with high and maximum containment research facilities. Such a commitment requires these research institutions to have the appropriate personnel for ensuring institutional compliance with pertinent Federal biosafety/biocontainment regulations and guidelines, and for overseeing the institution's biosafety and biocontainment management programs. In addition to these personnel, institutions also must ensure that sufficient resources are available for effective and comprehensive oversight of all activities related to high or maximum containment research.

Short-term steps:

- Require that all high and maximum containment research facilities owned or funded by the Federal Government designate a senior institutional official and a credentialed biosafety professional as described above and in Recommendation 3.3 (as it pertains to biosafety professionals)

Long-term steps:

- Determine what legal mechanism(s) would be needed to require that all high and maximum containment research facilities not owned or funded by the Federal Government designate a senior institutional official and a credentialed biosafety professional as described above

- Require that all high and maximum containment research institutions in all sectors be accountable to the Federal Government

OBJECTIVE 1 − Issue 1.4: Many institutions where high or maximum containment research is conducted have a properly constituted and functioning biosafety review committee or equivalent, although there is no universal requirement for these risk-assessment and review entities at the local (institutional) level. Under current Federal requirements, IBCs are only mandated to review research involving recombinant DNA (rDNA), and have to be established only at institutions that receive funding from NIH for such research or from other Federal agencies that have adopted the *NIH Guidelines* as a term and condition of funding for rDNA research.

To address this issue, the Task Force considered requiring risk assessments of all protocols potentially requiring high or maximum containment by a biosafety review committee or equivalent at all BSL-3, BSL-4 and equivalent agricultural containment research facilities in all sectors.

Considerations:

- Could help ensure that containment levels, laboratory safety practices, and risk management are based on thorough risk assessments
- Could help ensure the consistent application of proven biosafety/biocontainment practices and protective measures that are commensurate with risk
- Could help improve public confidence and trust that research in high and maximum containment research institutions in the United States undergoes consistently thorough review, and that risk is mitigated as effectively as possible
- Could help raise awareness among all laboratory personnel of the need for appropriate biosafety and biocontainment practices and procedures
- May have minimal impact on many institutions because:
  - A mechanism for reviewing research protocols is already in place at many high and maximum containment research institutions
  - Most high or maximum containment laboratories already have training programs in place to educate laboratory and support personnel about the risks associated with each research protocol and appropriate procedures to follow
- May not have an appropriately constituted and effective biosafety review committee or equivalent at some institutions
- May need to develop additional mechanisms at the Federal and local levels to provide guidance on risk assessment (e.g., development of a performance-based standard for biosafety review committees, and a template to highlight key provisions on how to conduct an acceptable risk assessment of protocols potentially requiring high or maximum containment) and risk management

- May require new regulatory authority for enforcement at entities not owned or funded by the Federal Government

The Task Force also considered the possibility of not mandating that a properly constituted and functioning biosafety review committee or equivalent review all protocols potentially requiring BSL-3, BSL-4, or equivalent agricultural containment. Pursuing this strategy is less desirable, given the consensus that the most important level of biosafety and biocontainment oversight occurs within individual research institutions, and a biosafety review committee or its equivalent is a fundamental component of effective local biosafety/biocontainment management systems.

RECOMMENDATION 1.4: Require that, at all institutions conducting high or maximum containment research, an appropriately constituted review body performs a thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment.

Rationale: It is critical that all high and maximum containment research institutions in all sectors (government [Federal, State, Tribal, and municipal], academia, privately funded research institutions, and private industry) thoroughly assess the risks of research conducted in their laboratories. The proper review of research protocols consists of a formal risk assessment, and competent personnel to determine the level of risk posed by each protocol. Although the Federal Government has provided guidance for these risk assessments (in the *BMBL*, and the *NIH Guidelines*), the assessments occur at individual research institutions[105] (i.e., at the local level).

Short-term steps:

- Where needed, provide additional guidance for risk assessments of laboratory protocols to help clarify and harmonize information in the *BMBL* and that of other relevant Federal regulations and guidelines[106]
- Mandate that all high and maximum containment research institutions owned or funded by the Federal Government have a properly constituted and functioning biosafety review committee or equivalent, and that a credentialed (certified or registered) biosafety professional (see also Recommendation 3.3) serves on the committee

[105] All institutions that conduct laboratory protocol risk assessments must have the resources and mechanisms to mitigate risks, as identified in the *BMBL*. These include assigning the appropriate biosafety level (BSL) for working with hazardous biological agents under specific laboratory protocols, identifying appropriate laboratory safety activities and procedures, ensuring on-site occupational health resources, etc.

[106] The key Federal regulations and guidelines that pertain to research activities at high and maximum containment facilities are the applicable Occupational Safety and Health Administration (OSHA) regulations (*General Duty Clause, Personal Protective Equipment Standards,* and *Bloodborne Pathogens Standard*), *Select Agent Regulations*, USDA/APHIS permitting regulations, *NIH Guidelines*, and the *BMBL*. For more information about Federal biosafety/biocontainment regulations and guidelines, accompanying guidance documents, and relevant standards, see Chapter III.

- Make biosafety and biocontainment risk assessments by a biosafety review committee or its equivalent a requirement for all Federally supported high and maximum containment research institutions

Long-term steps:

- Determine what legal mechanism(s) would be necessary to mandate that all high and maximum containment research institutions in all sectors have a properly constituted and functioning biosafety review committee or equivalent, and that a credentialed biosafety professional serves on the committee
- Determine what legal mechanism(s) would be necessary to make risk assessments of research protocols by a biosafety review committee or equivalent a requirement for all high and maximum containment research institutions in all sectors (i.e., including entities not owned or funded by the Federal Government)
- Implement the necessary legal mechanisms to ensure that, at all institutions conducting high or maximum containment research, an appropriately constituted review body performs a thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment

Summary of Recommendations to Address Objective 1	
Objective 1	**Recommendations**
Enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research through improved coordination of oversight activities.	1.1: Identify or establish a Federal entity to coordinate biosafety and biocontainment oversight activities, and to ensure comprehensive and effective Federal oversight for all high and maximum containment research facilities and activities in all sectors.
	1.2: Develop a registry of all high and maximum containment research facilities in the United States.

	1.3: Require that all institutions conducting high and maximum containment research designate: (1) a senior official with the appropriate knowledge, authority, and accountability who is responsible for institutional compliance with biosafety and biocontainment regulations and guidelines; and (2) a credentialed biosafety professional (see Recommendation 3.3) who is responsible for oversight of biosafety and biocontainment programs.
	1.4: Require that, at all institutions conducting high or maximum containment research, an appropriately constituted review body performs a thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment.

VI. CULTURE OF ACCOUNTABILITY AND COMPLIANCE

OBJECTIVE 2: Encourage a robust culture of accountability characterized by individual and institutional compliance with biosafety and biocontainment regulations, guidelines, standards, and policies.

A second objective for optimizing biosafety and biocontainment oversight is encouraging a culture of increased accountability and compliance with biosafety and biocontainment regulations, guidelines, standards, and policies by all individuals and institutions engaged in high or maximum containment research. A closely related goal is the development of mechanisms by which individuals and the institutions in which they work are encouraged to implement and adhere to biosafety/biocontainment regulations, guidelines, standards, and policies in ways that further enhance safety and reduce risk. Achieving this second objective will require strong support for local biosafety/biocontainment management programs from all levels of management at individual institutions where the research is conducted. It also may be necessary to improve existing mechanisms designed to ensure compliance.

At the level of individual research facilities, oversight entities such as a biosafety review committee or its equivalent need to have the institutional authority to enforce compliance with their decisions and applicable policies and requirements. At the Federal level, there needs to be a range of actions that can be taken to help ensure a culture of increased accountability and compliance.

Currently, all research institutions in all sectors covered by the Occupational Safety and Health Administration (OSHA) must comply with regulations promulgated by OSHA to ensure a safe workplace (OSHA *General Duty Clause* and *Bloodborne Pathogens Standard*). OSHA provides compliance directives that contain information about the interpretation of its regulations.[107] Enforcement mechanisms also are in place for ensuring compliance with Federal biosafety and biocontainment regulations and requirements that are specific to research and related activities at high and maximum containment research facilities. These include the *Select Agent Regulations* developed by the Department of Health and Human Services (HHS) Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS); APHIS permitting regulations; and the *NIH Guidelines for Research Involving Recombinant DNA Molecules* [*NIH Guidelines*]), which were developed by the HHS National Institutes of Health (NIH).

Potential Accreditation of Biosafety/Biocontainment Management Programs

[107] For the OSHA compliance directive on the *Bloodborne Pathogens Standard*, see http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=DIRECTIVES&p_id=2570.

One potential mechanism for encouraging a culture of increased accountability and compliance with biosafety and biocontainment standards is to establish an accreditation system[108] for the review and/or inspection of biosafety/biocontainment management programs at individual high and maximum containment research institutions. Accreditation would allow the institution to demonstrate that its biosafety and biocontainment programs meet or exceed national standards. Any decision to require laboratory accreditation would need to be accompanied by a clear biosafety/biocontainment management standard and an indication of what entity (entities) would serve as an accrediting body. A feasibility study of the issue of accreditation could be undertaken by a representative group of Federal and non-Federal stakeholders. (For a more complete discussion of a potential accreditation system for biosafety management systems at high and maximum containment research laboratories, see Appendix G.)

Issues, Options, and Recommendations to Address Objective 2

OBJECTIVE 2 − Issue 2.1: Individuals and institutions must comply with Federal biosafety/biocontainment regulations and standards, as appropriate, if they work with select agents or toxins, bloodborne pathogens, or agents covered by the APHIS permitting system. Also, the *NIH Guidelines* apply to any project involving rDNA that is conducted at or sponsored by an entity that receives support for such research from NIH or from other Federal agencies that require compliance with the *NIH Guidelines*. Even if a project is entirely privately funded, it is subject to the *NIH Guidelines* if any investigator at the institution or the company funding the project has a grant or contract from the NIH for rDNA research.

However, a small portion of research with hazardous biological agents conducted in high and maximum containment facilities is not subject to Federal biosafety/biocontainment regulations and other requirements (e.g., institutions in the academic or private sector that do not receive Federal funding and are not engaged in research on the agents just noted). And, although compliance with the *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*) is widespread, compliance is voluntary for some BSL-3 and equivalent agricultural containment laboratories, and therefore can be subject to wide interpretation.[109] This creates a gap, although small, in mandatory compliance (and Federal oversight) for non-Federally owned or funded institutions that work with non-

[108] For the purposes of this report, the term "accreditation" refers to an objective assessment by an independent body of an institution's biosafety/biocontainment or biorisk management program.

[109] All BSL-4 and equivalent containment facilities possess, use, or transfer select agents, and these facilities are required to comply with the *Select Agent Regulations*. The *Select Agent Regulations* cite the *BMBL* but do not require adherence to it, although many Federal agencies require their own laboratory personnel to comply with it and recognize the *BMBL* as the minimal performance standard. Also, many BSL-3 and equivalent agricultural containment research facilities that do not work with select agents comply voluntarily with the biosafety/biocontainment guidance contained in Federal guidelines and related documents, such as the *BMBL* and *NIH Guidelines*.

select agents, non-recombinant agents, non-bloodborne agents, and agents not covered by the APHIS permitting system.

To address this issue, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) considered two options:

> **Option A: Mandate compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.**
> **Option B: Encourage compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.**
>
> *Considerations for Option A:*
> - Would utilize the *BMBL* and the *NIH Guidelines* as the basis for compliance by all high and maximum containment research institutions, thus reducing potential inconsistencies in laboratory practices and procedures
> - Would provide a basis for enforcing adherence to good laboratory practices and procedures
> - Would not be burdensome to most high and maximum containment research institutions because these institutions already comply with the *BMBL* and the *NIH Guidelines*
> - Would provide a consistent foundation for laboratory risk assessments and improvements in risk-management methodology, as needed

The Task Force considered Option B, but elected not to pursue it. Option B, to "encourage" compliance with the *BMBL* and the *NIH Guidelines*, rather than require compliance, would not represent a significant improvement over the current, voluntary system. Therefore, the Task Force recommends Option A because it helps ensure the consistent application of good laboratory practices that are most likely to protect the safety of laboratory personnel, the public, agriculture, and the environment. Also, mandating compliance with the *BMBL* and the *NIH Guidelines* helps strengthen the current system of oversight.

RECOMMENDATION 2.1: Mandate compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.

Rationale: The *BMBL* and *NIH Guidelines* provide information about working safely with hazardous biological agents at all biosafety levels (BSL-1 through BSL-4 and equivalent agricultural containment facilities[110]), and many Federal agencies currently

[110] Equivalent containment facilities include animal biosafety levels (ABSL-1, ABSL-2, ABSL-3, and ABSL-4), BSL-3 "enhanced," and biosafety level-3-agriculture (BSL-3-Ag).

mandate compliance with the *BMBL*. It is important that individuals at all biocontainment facilities in all sectors comply with the same safety and containment regulations, guidelines, standards, and policies as appropriate. This recommendation would require *all* high and maximum containment research facilities, regardless of their funding sources, to comply with the *BMBL* and *NIH Guidelines*. Compliance with Federal biosafety and biocontainment guidelines also would serve as a foundation for carrying out risk assessments of all research protocols in BSL-3, BSL-4, and equivalent agricultural containment facilities. Implementation of this recommendation needs to provide sufficient flexibility and adaptability to keep pace with evolving science.

Short-term steps:

- Mandate compliance with the *BMBL* and the *NIH Guidelines* as a term and condition of funding for all Federally funded high and maximum containment research facilities[111]
- Encourage compliance among individuals and institutions not in receipt of Federal funds until such time that compliance is mandated in all sectors

Long-term steps:

- Extend the compliance requirement (based on new or expanded legislative authority, as needed) to non-Federally owned or funded high and maximum containment research facilities

OBJECTIVE 2 − Issue 2.2: Currently, there is no standardized mechanism for evaluating biosafety and biocontainment management programs at high and maximum containment research facilities, or for assuring that biosafety and biocontainment guidelines, standards, and policies are being followed. Needed is a system to ensure these activities occur.

To address this issue, the Task Force considered three options:

Option A: Determine the feasibility and advisability of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions.

Option B: Support the development of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions

Option C: Establish a Federal permitting or licensure program to help ensure that high and maximum containment facilities comply with biosafety and biocontainment guidelines, standards, and policies.

Considerations for Option B:

- Would require collaboration among key Federal and non-Federal stakeholders who could help develop accreditation standards and an

[111] Mandatory compliance with the *BMBL* for a high containment greenhouse would not be relevant because the *BMBL* does not cover these facilities.

accreditation system, and entities that would be affected by an accreditation process

- Would provide an objective assessment of an institution's biosafety/biocontainment management program and help assure that it meets national standards, if accredited
- Could be coupled with the development of mechanisms to encourage personnel and institutions with high or maximum containment research facilities to use accreditation standards as the basis for further enhancing safety and reducing risk posed by work with hazardous biological agents
- If an accreditation system were implemented, it should:
  - Raise awareness about and help increase compliance with relevant biosafety and biocontainment guidelines, standards, and policies
  - Yield valuable information about current adherence to biosafety and biocontainment guidelines, standards, and policies, and help identify areas in which personnel training should be improved
  - Help demonstrate evidence of a nationwide commitment to excellence in biosafety/biocontainment practices and procedures, help enhance the culture of accountability and compliance, provide an oversight mechanism, and help enhance public trust

The Task Force decided to recommend Option B, to support the development of an accreditation system. Inherent in the implementation of Option B would be conducting the kind of feasibility study described in Option A, i.e., generating important information about accreditation standards and an accreditation system for high and maximum containment research institutions, and bringing together the entities best qualified to address these issues. Any accreditation standards or system that emerges from this collaborative process will be more likely to achieve the overall goals of improving biosafety and biocontainment oversight without impeding progress in scientific research. The Task Force decided not to recommend Option C, because doing so would necessarily broaden the scope of current licensing or permitting programs—e.g., the permitting program used by USDA/APHIS—and require human, financial, and Federal agency resources that currently are not available.

RECOMMENDATION 2.2: Support the development of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions.

Rationale: An accreditation system[112] for biosafety/biocontainment management programs at all institutions with high and maximum containment research facilities in all sectors could help achieve many objectives identified in this report, which include:

[112] An accreditation system for biosafety/biocontainment management programs could addresses biosafety and biocontainment facilities, equipment (for primary and secondary containment), laboratory procedures, mechanisms for risk assessment, personnel competency and training, incident-reporting procedures, occupational health resources, emergency response measures, etc.

- Enhancing the culture of individual and institutional accountability, and ensuring compliance with biosafety/biocontainment regulations, guidelines, standards, and policies (Objective 2)
- Assisting stakeholders in understanding the biosafety and biocontainment criteria their institutions are required to meet (Objective 2)
- Ensuring that relevant staff are appropriately trained and technically competent (Objective 3)
- Determining whether laboratory incidents are being reported, as appropriate (Objective 4)
- Determining whether the infrastructure of high and maximum containment research facilities is being adequately maintained to ensure the safety of these laboratories (Objective 6)
- Enhancing public trust (Objective 8)

Before an accreditation system could be designed, standards for accreditation must be developed. Accreditation standards and an accreditation system for high and maximum containment research institutions could be modeled after existing accreditation standards and systems used by international organizations,[113] and the draft laboratory biorisk management standard developed by the European Committee for Standardization, also known as CEN.[114] Model accreditation standards and systems developed by U.S. organizations include those for health care (Joint Commission),[115] pathology laboratories (College of American Pathologists),[116] and animal research facilities (Association for Assessment and Accreditation of Laboratory Animal Care [AAALAC]).[117]

Accredited biosafety/biocontainment management programs would demonstrate evidence of institutional commitment to excellence in biosafety and biocontainment practices and

[113] The *WHO Laboratory Biosafety Manual – Third Edition 2004* is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf. The NIH requirements are more precise with regard to the standards that must be met including actual validation of engineering and HVAC controls. Certification of intramural high-containment laboratories at NIH is performed by a team of professionals with experience and credentials in engineering and biosafety/occupational safety and health.
[114] CEN is the European Committee for Standardization, or Comité Européen de Normalisation. The CEN laboratory biorisk management standard, CWA 15793:2008, was prepared by CEN Workshop 31 - Laboratory Biosafety and Biosecurity and is available at http://www.cen.eu/cenorm/sectors/technicalcommitteesworkshops/workshops/ws31.asp.
[115] The Joint Commission is an independent, not-for-profit organization that accredits and certifies more than 15,000 health care organizations and programs in the United States. For more information, see http://www.jointcommission.org/AboutUs/.
[116] For information about laboratory accreditation by the College of American Pathologists, see http://www.cap.org/apps/cap.portal?_nfpb=true&_pageLabel=accreditation. For information about accreditation programs of the National Accrediting Agency for Clinical Laboratory Sciences, see http://www.naacls.org/accreditation/.
[117] The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. For information about AAALAC, see: http://www.aaalac.org/about/index.cfm.

procedures, demonstrate accountability and compliance, and provide evidence of an effective oversight mechanism.

Short-term steps:

- Review and evaluate relevant laboratory accreditation standards and existing model systems of accreditation to determine whether aspects of these models could be used as a basis for developing accreditation standards and an accreditation system for biosafety/biocontainment management programs at all high and maximum containment research facilities
- Work with stakeholders to develop appropriate accreditation standards and the optimal parameters of an accreditation system for biosafety/biocontainment management programs at individual high and maximum containment research institutions[118]

Long-term steps:

- Work with stakeholders to design and implement the accreditation system for all high and maximum containment research facilities
- Develop additional mechanisms, if necessary, to encourage institutions with high or maximum containment research facilities to participate in the accreditation process

Summary of Recommendations to Address Objective 2	
Objective 2	**Recommendations**
Encourage a robust culture of accountability characterized by individual and institutional compliance with biosafety and biocontainment regulations, guidelines, standards, and policies.	2.1: Mandate compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.
	2.2: Support the development of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions.

[118] The effort could include collaborations to establish requirements for Approved Accrediting Organizations (AAO), an approach used by HHS Centers for Medicare and Medicaid Services (CMS) to accredit healthcare organizations, laboratories, and ambulatory care facilities, etc., as Medicare providers

VII. TRAINING AND COMPETENCY

OBJECTIVE 3: Develop a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories.

It is important to ensure that all personnel who work in, oversee, support, or manage high or maximum containment research laboratories achieve and maintain a sufficient level of technical competence for maintaining safety in these facilities. Putting into practice mechanisms to accomplish this goal also should help ensure the availability of an adequate number of highly trained individuals, particularly at high and maximum containment research facilities that are expanding or are under construction. Efforts to develop or increase the capacity of training programs could encompass mechanisms for improving their scope, content, and availability, as needed.[119,120]

Meeting this objective will require the development of minimum training standards and core competencies, a comprehensive training strategy, and procedures for documenting that training has occurred and technical competency has been achieved. The need for core competencies and training standards applies to all personnel who work in, oversee, support, or manage high or maximum containment research facilities including: (1) principal investigators (PIs), laboratory supervisors, researchers, and technicians (including those with and without formal training in laboratory safety, and any students who work in BSL-3 facilities),[121] (2) animal care and support staffs (including security and housekeeping staff); (3) facilities and engineering staff (including those who maintain the associated systems of these facilities such as the specialized air-flow systems that are specific to high and maximum containment laboratories); (4) institutional biosafety professionals (biosafety officers [BSOs] and their equivalents) and

[119] Improving the scope of training and certification programs means ensuring that minimum competency standards and training and certification programs have been developed for all categories of essential personnel. Efforts to improve the content (curricula) of these programs will require consultation and collaboration with stakeholders and the entities that offer the training and certification programs (individual research institutions, and professional societies and associations). Improving the availability of training and certification programs means ensuring that a sufficient quantity of training and certification programs is available to all categories of essential personnel.

[120] In draft legislation to reauthorize the *Select Agent Program and Biosafety Improvement Act of 2009* (S. 3127 and H.R. 1225), the U.S. Senate and House of Representatives include language on training laboratory personnel. Also, high and maximum containment research laboratories must follow training and information requirements in applicable OSHA standards (e.g., OSHA standards on PPE, Respiratory Protection, Bloodborne Pathogens, Hazard Communication, and Laboratories).

[121] For a discussion of training for BSL-4 personnel, see the Perspective by Le Duc JW, et al., Framework for Leadership and Training of Biosafety Level 4 Laboratory Workers. *EID*. November 2008. 14 (11) 1685–88, available at http://www.cdc.gov/EID/content/14/11/1685.htm.

members of biosafety review committees (institutional biosafety committees [IBCs] and their equivalents); (5) individuals, including senior institutional officials, who have overall management responsibilities for these facilities; and (6) individuals who review and inspect the facilities.

The personnel associated with high and maximum containment research laboratories play different roles in a laboratory's biosafety management system. Therefore, any proposal to require specific training and/or certification for these individuals would need to take into account an individual's level of responsibility for laboratory biosafety and biocontainment. Institutional biosafety professionals, for example, need to attain a broader and more extensive level of biosafety and biocontainment expertise than do PIs and other laboratory scientists who focus on the hazards presented by the particular agents and operations within their specific laboratory or work areas. A tiered approach to biosafety training requirements commensurate with job responsibilities should help address this issue. The approach could include core training for each position and specific training that is tailored to the facility, agents under study, and the work being done.

All training of laboratory personnel should be planned and managed at the local (institutional) level, and take into account the needs and resources of the individual institution. Although professional organizations and institutions can provide assistance with training on certain elements of biosafety and biocontainment, agent- and site-specific training also is required because risk assessments take place locally and protocol-specific safeguards need to be implemented.

Institutional training programs could be reviewed by biosafety review committees (IBCs and equivalents) with approval from relevant institutional officials, taught within individual laboratories or by outside organizations, and subject to oversight. Laboratory PIs or supervisors should assume responsibility for ensuring that effective training takes place. After initial training, relevant personnel should receive annual retraining specific for their positions. In addition, training should be performed whenever a significant change in laboratory operations occurs. Senior institutional officials could provide "assurances" to the appropriate authorities that all relevant employees are appropriately trained and technically proficient (see Recommendation 1.3).

Credentialing of personnel by an outside body is desirable, when available and appropriate. BSOs and equivalent biosafety professionals should be credentialed (certified or registered), because they have broad biosafety/biocontainment oversight responsibility for all the research activities at a high or maximum containment facility. A credentialed biosafety professional should be responsible for oversight of biosafety and biocontainment programs at all high and maximum containment research facilities in all sectors (see Recommendation 1.3). Because the nature of the scientific endeavor is constantly evolving and many non-biologists are using tools and methods involving hazardous biological agents, it might also be necessary to develop different kinds of education programs to meet the specific needs of researchers who do not have backgrounds in laboratory biosafety/biocontainment practices and procedures (e.g., chemists, biochemists, and geneticists), as well as programs for students who seek

biosafety training or who work in BSL-3 facilities. Also important is the establishment of standardized methods to evaluate and improve, if needed, the effectiveness of existing training and certification programs.

Issues, Options, and Recommendations to Address Objective 3

OBJECTIVE 3 – Issue 3.1: There are no minimum national, position-specific training standards or core competencies in biosafety and biocontainment for all personnel who work in, oversee, manage, or support research and related activities at high and maximum containment laboratories in all sectors.

To address this issue, the Task Force considered the option of establishing training standards and core competencies in biosafety and biocontainment for all research, managerial, oversight, and support personnel at high and maximum containment research laboratories in all sectors. The training standards and core competencies should reflect the responsibilities of the specific functions and responsibilities associated with each position. Participants at the public meeting held December 8−9, 2008, encouraged the Task Force to recommend the development of training standards and core competencies in biosafety and biocontainment.

Considerations:

- Would identify appropriate levels of expectation about personnel training and competence
- Would help ensure consistency in training
- Could provide reassurance to the public and enhance public trust if training standards and core competencies were established
- Would probably require phasing-in of training standards and core competencies
- May require new statutory and/or regulatory authority

The Task Force also considered and rejected the possibility of not establishing training standards and core competencies, i.e., of maintaining the *status quo*. Although many, if not most, personnel who work, oversee, or manage high and maximum containment facilities are appropriately trained and technically competent, it is important to ensure that all personnel meet desirable standards and attain competence commensurate with their job responsibilities.

RECOMMENDATION 3.1: Establish national, position-specific training standards and core competencies in biosafety and biocontainment for all research, managerial, and support personnel at high and maximum containment research laboratories in all sectors.

Rationale: The Federal Government and individual research institutions share responsibilities for ensuring that all research, oversight, managerial, and support personnel at all high and maximum containment research laboratories in all sectors are adequately trained and technically competent. Establishing core biosafety and biocontainment training standards and core competencies[122] for these personnel will help ensure that laboratory and support personnel are working safely, and that personnel responsible for oversight and management are knowledgeable about the safety risks and how to mitigate them. The standards would also help improve consistency in laboratory and oversight practices, and establish minimum criteria for training.

Short-term steps:

- Work with stakeholders to develop core competencies and position-specific training standards for all research, oversight, managerial, and support personnel at high and maximum containment research laboratories.
- Develop a mechanism to utilize information from facility incidents and inspections to inform the development of standards for biosafety/biocontainment training and competencies

Long-term steps:

- Work with stakeholders (including individual research institutions) to develop a comprehensive training strategy for biosafety and biocontainment and a national implementation plan
- After core training standards and core competencies for biosafety and biocontainment are developed, include them in the *BMBL* and other Federal guidance documents
- Develop a national strategy that includes training standards and core competencies, as well as mechanisms to evaluate and improve them, as necessary

OBJECTIVE 3 – Issue 3.2: There is a need to ensure that all personnel who work in high and maximum containment research facilities, including students and researchers who lack formal training in biosafety/biocontainment practices and procedures, are appropriately trained and competent in biosafety and biocontainment practices and procedures. Training programs for these personnel are offered by the Federal Government, professional societies, and individual research institutions. (See Appendix

[122] Core Training: General biosafety awareness about biosafety levels, aseptic technique, biosafety cabinet operation and use, disinfection and decontamination methods. The training needs to meet requirements of Federal regulations, as appropriate (Occupational Safety and Health Administration [OSHA] General Duty Clause and *Bloodborne Pathogens Standard,* Department of Transportation [DOT] and International Air Transport Association [IATA] shipping regulations, hazard communication plan, and *Select Agent Regulations*). Specific Training: Routes of transmission of infectious agents used on site; and site-specific work practices (unique signs and labels, personal protective equipment, other protective equipment and engineering controls, equipment operation, facility design, security procedures, waste disposal, special laboratory practices, medical surveillance programs, immunization requirements, laboratory specific emergency response procedures, incident reporting procedures, decontamination procedures, etc.).

H for a representative listing of training and certification programs offered by professional organizations and other entities.)

To address this issue, the Task Force discussed the need for high and maximum containment research facilities to ensure that all members of their workforce, including students and scientists who have not received formal laboratory safety training, are appropriately trained and competent.

Considerations:

- Would help ensure that all personnel who work in, oversee, support, or manage high and maximum containment research facilities meet national training standards and attain core competencies
- Would heighten awareness of biosafety/biocontainment practices and procedures in laboratories used by students and science faculty, as well as by personnel in high and maximum containment research laboratories
- Could provide an assurance that staff who support high and maximum containment research environments acquire and maintain the knowledge and skills necessary to meet the biosafety and biocontainment challenges associated with the conduct of research in these facilities
- Could help improve the quality and consistency of biosafety and biocontainment training
- Determine the legal mechanisms for imposing this requirement on all high and maximum containment research facilities

The Task Force debated whether institutions should be required to ensure that all members of their workforce for high and maximum containment research laboratories were appropriately trained and competent, and decided that such an assurance would be beneficial. The Task Force also discussed whether the biosafety/biocontainment training programs offered by educational institutions and professional organizations are sufficient, and decided that a careful review of these programs is needed.

RECOMMENDATION 3.2: Require institutions to ensure that all individuals who work in, oversee, support, or manage high or maximum containment research laboratories are appropriately trained and competent in biosafety and biocontainment.

Rationale: Requiring institutions to ensure that all individuals who work in, oversee, support, or manage their high or maximum containment research laboratories are appropriately trained and competent means that institutions need to provide a formal assurance that biosafety and biocontainment training of all relevant personnel has occurred. Training programs for personnel at high and maximum containment research laboratories are offered by the Federal Government, professional societies, individual research and educational institutions, and other entities.

Short-term steps:

- Determine the parameters for institutions to provide assurance that all individuals who work in, oversee, support, or manage their high or maximum containment research laboratories are appropriately trained and competent
- Develop a resource that lists current, broadly available training programs offered by the Federal Government, professional societies, and individual research and educational institutions. An entity (perhaps the centralized Federal entity described in Recommendation 1.1) could establish an information clearinghouse that contains this information
- Review the current and anticipated personnel needs of high and maximum containment research laboratories to determine whether current, broadly available training programs (offered by the Federal Government, professional societies, and individual research and educational institutions) have sufficient capacity to meet training needs

Long-term steps:

- Determine whether imposing this new requirement that high and maximum containment research institutions provide assurance their personnel are appropriately trained and competent requires new statutory and/or regulatory authority
- Require that all high and maximum containment research facilities in all sectors ensure that all individuals who work in, oversee, support or manage high or maximum containment research laboratories are appropriately trained and competent, and meet national standards for core training and competency (as described in Recommendation 3.1)
- Determine the legal mechanisms for imposing this requirement on all high and maximum containment research facilities

OBJECTIVE 3 – Issue 3.3: There is no uniform requirement that biosafety professionals (BSOs and their equivalents) who oversee the biosafety management programs at high and maximum containment research facilities are credentialed (certified or registered), although many of these individuals are credentialed. Current credentialing programs for biosafety professionals are voluntary. (See Appendix H for examples of certification and registration programs for biosafety professionals.)

To address this issue, the Task Force considered three options:

OPTION A: Implement a phased-in requirement for a credentialed (certified or registered) biosafety professional to be responsible for oversight of biosafety and biocontainment management programs at every high or maximum containment research facility.

OPTION B: Mandate certification or registration for biosafety professionals at all high and maximum containment research institutions.

OPTION C: Strongly encourage biosafety professionals at high and maximum containment research institutions to be credentialed.

Considerations for Option A:

- Would enhance the consistency and quality of performance by biosafety professionals (BSOs and their equivalents) who are responsible for the oversight of biosafety/biocontainment management systems at high and maximum containment research facilities
- Would increase the effectiveness and credibility of institutional biosafety/biocontainment management programs
- Could enhance public trust by showing that a credentialed biosafety professional is responsible for oversight of biosafety/biocontainment management programs at every high or maximum containment research facility
- Could require the development of incentives (e.g., "time off the job" for biosafety professionals who seek certification or registration) to implement
- May require new statutory and/or regulatory authority

After extensive discussion, the Task Force decided not to recommend option B or C. Option B, to mandate that all biosafety professional at high or maximum containment research facilities be credentialed, might be impossible for some institutions to achieve immediately because of insufficient resources or the lack of a consistent need for an on-site credentialed professional (i.e., if only one laboratory at the institution operates as a BSL-3 facility, or operates at that level on an intermittent basis). Option C, to encourage, rather than require, all BSL-3 or equivalent research facilities to have a credentialed biosafety professional, would fail to result in a marked improvement over the existing system of biosafety/biocontainment oversight.

Because not all biosafety professionals are currently credentialed, the Task Force recommends Option A, to implement a phased-in requirement for a credentialed (certified or registered) biosafety professional (BSO or equivalent) to be responsible for oversight of biosafety/biocontainment management programs at every high or maximum containment research facility. The consistency and effectiveness of biosafety/biocontainment oversight at the local (institutional) level is fundamental to the overall biosafety/biocontainment oversight framework, and biosafety professionals (see Recommendation 1.3)—as well as institutional biosafety review committees (see Recommendation 1.4)—play a critical role in local oversight. Participants at the public meeting held December 8−9, 2008, supported this recommendation and emphasized the need for a fully trained biosafety professional at BSL-3, BSL-4, and equivalent agricultural containment research facilities.

RECOMMENDATION 3.3: Implement a phased-in requirement that the designated biosafety professional (Biological Safety Officer or equivalent) at all high and maximum containment research facilities be credentialed.

Rationale: Credentialed biosafety professionals (BSOs and their equivalents) provide critical guidance and oversight for work with hazardous biological agents and toxins. The ideal situation is that all institutions with high or maximum containment research laboratories have an on-site or otherwise accessible biosafety professional, and that these individuals are highly qualified and credentialed (certified or registered).[123] (See also Recommendation 1.3.)

The Task Force recommends instituting a phased-in process to ensure that the designated biosafety professional (BSO or equivalent) at all high and maximum containment research facilities become credentialed. Although the initial goal is to promote training and credentialing of these individuals, the ultimate goal could be to mandate that all high and maximum containment research institutions have at least one credentialed biosafety professional (BSO or equivalent). Based on experience with Animal Care and Use Committees and other laboratory-associated entities, the Task Force realizes this process may take many years.

Short-term steps:

- Initiate a study to explore the feasibility of requiring that the designated biosafety professional (BSO or equivalent) is credentialed (certified or registered)
- Establish a program to allow biosafety professionals to gain practical experience working as technicians or scientists in high and maximum containment research laboratories
- Review current and future needs for biosafety professionals, and work with professional societies to develop mechanisms to increase the pool of credentialed biosafety professionals
- Determine whether relevant Federal agencies could support training to facilitate this goal
- Expand biosafety training and certification programs offered by the Federal Government (e.g., the National Biosafety and Biocontainment Training Program [NBBTP] at NIH),[124] by professional organizations, or by the private sector
- Develop incentives for biosafety professionals to become credentialed

Long-term steps:

- Phase in the requirement for certification or registration, because not all biosafety professionals have these credentials, and the certification/registration process would take time to implement

[123] Achieving this goal immediately might not be feasible, but should be possible within 5 years.
[124] For more information about the NBBTP, see http://www.nbbtp.org/nf_home.cfm.

- Determine any additional training requirements that might be necessary for biosafety professionals to be able to oversee research activities at BSL-3, BSL-4, and equivalent agricultural facilities
- Determine the legal options for imposing this new requirement

Summary of Recommendations to Address Objective 3	
Objective 3	**Recommendations**
Develop a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, or manage high or maximum containment research laboratories	3.1: Establish national, position-specific training standards and core competencies in biosafety and biocontainment for all research, managerial, and support personnel at high and maximum containment research laboratories in all sectors.
	3.2: Require institutions to ensure that all individuals who work in, oversee, support, or manage high or maximum containment research laboratories are appropriately trained and competent in biosafety and biocontainment.
	3.3: Implement a phased-in requirement that the designated biosafety professional (BSO or equivalent) at all high and maximum containment research facilities be credentialed.

VIII. INCIDENT-REPORTING, ANALYSIS, AND INFORMATION-SHARING

OBJECTIVE 4: Obtain and analyze information about laboratory incidents to enable trend analysis, minimize the number of future incidents, and share lessons learned, with the overall goals of optimizing laboratory safety and oversight.

Prompt and detailed reporting of incidents[125] involving high and maximum containment research is essential to optimizing laboratory safety and oversight. Although the overall goals are to improve laboratory safety and oversight, including understanding why incidents occurred and how they can be prevented in the future, other goals are to provide a resource for generating and sharing lessons learned. Analyses of reports of biosafety and biocontainment incidents, or noncompliance with mandated or recommended safety practices also could point to the need for additional training, new or revised guidelines or practices, site visits or inspections, and provide essential information for public education and outreach (e.g., that a laboratory incident is not equivalent to a public health risk).

Achieving these goals will be facilitated by:

- Developing a clear and consistently applied definition of what constitutes an incident that must be reported[126]
- Further defining the purpose and key elements of any proposed, centralized system for obtaining and analyzing biosafety and biocontainment incidents that occur in high and maximum containment research facilities, and a mechanism for sharing lessons learned
- Determining whether an existing Federal entity could host and manage a nationwide incident-reporting system, or whether it is necessary to create a new Federal entity[127]
- Developing mechanisms to evaluate the effectiveness of and continually improve incident-reporting, analysis, and information-sharing

[125] "Incidents" would need to be defined for the purposes of this discussion, but could include laboratory accidents, significant exposures to biological hazards, and laboratory-acquired illnesses (LAIs). Some incidents are defined by regulation or included in guidelines (e.g., select agent incident-reporting; incidents/accidents with recombinant DNA).

[126] The Federal Select Agent Program has posted guidance for the regulated community on what constitutes a "reportable incident." For more information about the Select Agent Program, see http://www.selectagents.gov. Guidance documents for the Select Agent Program are available at http://www.selectagents.gov/complianceassistance.htm.

[127] Proposed legislation to reauthorize the Select Agent Program and improve oversight of high containment laboratories (S. 3127 and H.R. 1225) includes language to establish an incident-reporting system.

- Ensuring the existence of a comprehensive, integrated system to issue alerts in the event new threats to the safety of laboratory workers or public health are identified[128]

Proposed key elements and characteristics of a centralized incident-reporting system are: (1) that it has clearly defined protocols for incident-reporting; (2) is anonymous and non-punitive; (3) that follow-up to a reported incident should focus on corrective actions and lessons learned, rather than assigning blame; and (4) that the system is designed to yield benefits to individuals, research institutions, and the U.S. research enterprise. Such an incident-reporting system could include information from current mandatory reports, as appropriate. A Federal entity that hosts and manages such an incident-reporting system also could be responsible for ensuring the existence and effectiveness of a mechanism to issue alerts about new safety threats. (See Appendix I for more information about a potential, centralized incident-reporting system.)

A potential model for an incident-reporting system is the voluntary, non-punitive, centralized system used by the aviation industry. It promises anonymity and guarantees the Federal Aviation Administration (FAA) "... will not use reports submitted to the National Aeronautics and Space Administration (NASA) under the Aviation Safety Reporting Program (or information derived therefrom) in any enforcement action, except information concerning accidents or criminal offenses which are wholly excluded from the program."[129] A second incident-reporting system that could be used as a model is the Department of Health and Human Services (HHS) Agency for Healthcare Research and Quality (AHRQ) Patient Safety Organization-Network of Patient Safety Databases (PSO/NPSD).[130]

The goals of institutional incident-reporting (also known as internal reporting) differ in some respects from those of a potential, nationwide system (external reporting). However, information gathered through internal, institutional incident-reporting systems could be modified, as appropriate, and submitted to a nationwide, external incident-reporting system for analysis and sharing lessons learned.

Officials at various Federal agencies have discussed the costs and benefits associated with a nationwide system for incident-reporting and analysis, and methods to encourage participation. Further discussion is needed to ensure that a comprehensive, efficient approach is developed to manage information gleaned from the reporting of incidents.

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[128] An example of a new threat is the identification of a new zoonotic agent.

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

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

Issues, Options, and Recommendations to Address Objective 4

OBJECTIVE 4 – Issue 4.1: Although the OSHA record-keeping regulations,[131] *Select Agent Regulations* developed by HHS and the U.S. Department of Agriculture (USDA),[132] and *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*)[133] include requirements to report laboratory incidents, there is no centralized, integrated incident-reporting and analysis system for all U.S. high and maximum containment research facilities in all sectors.

To address this issue, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) explored whether to establish a new voluntary, non-punitive incident-reporting system for high and maximum laboratories that would ensure the protection of sensitive and private information, as necessary. If a new voluntary, non-punitive incident-reporting system is established, a centralized, integrated mechanism for analyzing incidents and sharing information and lessons learned from both current mandatory reports and the new voluntary reporting system could be developed.

Considerations:

- Could help provide timely incident-reporting and management
- Could provide a means for obtaining information about laboratory incidents that currently is not being obtained
- Could enhance transparency and public trust
- Could be used to promote and reinforce a culture of safety
- Could require incentives to encourage all high and maximum containment research laboratories in all sectors to report relevant incidents
- Would need to be integrated with existing incident-reporting systems
- Would require overcoming barriers to reporting incidents, including LAIs because of:
  - Lack of a clear definition of an incident and understanding of a reportable incident
  - Concern that information could be used as an enforcement tool
  - Lack of explicit, standardized incident-reporting protocols

[131] Most high and maximum containment research facilities are exempt from OSHA record-keeping regulations, because OSHA has classified them as having low overall recordable work-related injuries and illnesses, in comparison to the national average for all industries (see Chapter III and Appendix D).
[132] The *Select Agent Regulations* (7 CFR 331, 9 CFR 121, and 42 CFR 73) require reporting of the "theft, loss, or release" of a select agent or toxin. For the *Select Agent Regulations*, see http://www.selectagents.gov/.
[133] Section IV-B-2-b-(7) of the *NIH Guidelines* states that IBCs should report "...any significant problems, violations of the NIH Guidelines, or any significant research-related accidents and illnesses" to NIH OBA within 30 days. Appendix G of the *NIH Guidelines* specifies certain types of accidents that must be reported on a more expedited basis. For more information, see http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.

    - Lack of recognition or awareness that an event was an incident that should be reported, or an infection that may have been laboratory-acquired
    - Belief the report will: bring negative attention to an individual or institution; interrupt or delay work; cause personal, professional, institutional embarrassment; or result in a reprimand or loss of job
    - Belief that nothing will be done in response to an incident report
    - Lack of useful investigation, follow-up, or feedback
    - Fear of litigation
    - May require new statutory and/or regulatory authority
- Could provide a means for analyzing and sharing lessons learned with other high and maximum containment research facilities that are engaged in similar laboratory activities
- Could provide a means to obtain data on which to base improved risk assessments and risk management practices
- Could provide a scientific basis for improving biosafety regulations and guidelines, training programs, facility operations, equipment design, and safety maintenance
- Could be used to reduce any stigma associated with reporting laboratory incidents, if information is used frequently and for positive goals
- Could provide a means to identify trends, e.g., hazards associated with a particular type of equipment

The Task Force also considered whether the current systems of incident-reporting (e.g., those required by the Occupational Safety and Health Administration [OSHA], the *Select Agent Regulations*, and the *NIH Guidelines*) are sufficient to address current needs. After extensive discussion, Task Force members agreed that aspects of current reporting systems could be improved by establishing a new, centralized incident-reporting system. The Task Force recognizes the value of an incident-reporting system that is voluntary and non-punitive in nature.

If a new, centralized incident-reporting system is established, a mechanism for the analysis of information about laboratory incidents would be established, and include information from the new system as well as information from current mandatory reports, Sensitive and private information would be protected, as necessary. The Task Force agreed that analyzing information about laboratory incidents and sharing lessons learned could help improve overall laboratory safety and compliance with biosafety and biocontainment regulations, policies, standards, and guidelines. Several individuals endorsed this approach at the public meeting held December 8−9, 2008.

RECOMMENDATION 4.1: **Establish: (1) a new voluntary, non-punitive incident-reporting system for high and maximum containment research laboratories that would ensure the protection of sensitive and private information, as necessary; and (2) a centralized, integrated mechanism for analyzing incidents and sharing**

information and lessons learned from both current mandatory reports and the new voluntary reporting system.

Rationale: Reporting LAIs and other laboratory incidents with agents of greatest concern is a statutory requirement under the OSHA record-keeping regulations and the HHS/USDA *Select Agent Regulations.*[134] Reporting of rDNA incidents is also required as a term and condition of NIH funding under the *NIH Guidelines.* (For more information about existing incident-reporting systems, see Chapter III.) The establishment of new voluntary, non-punitive incident-reporting system for high and maximum research laboratories, and a centralized, integrated mechanism for analyzing incidents and sharing information and lessons learned from both mandatory reports and the new voluntary reporting system would make it possible to: (1) extract information from existing reporting systems (without duplicating efforts); (2) acquire and analyze additional information about relevant laboratory incidents; (3) share information and lessons learned with stakeholders, as appropriate; (4) improve safety and oversight at high and maximum containment research laboratories; (5) help determine why the incidents occurred and how they can be prevented in the future; (6) identify needs for additional or revised training of all individuals who work in, oversee, or manage high or maximum containment research laboratories; (7) provide information for improving or creating biosafety/biocontainment regulations, guidelines, standards, or policies; and (8) provide essential information for public education and outreach. A centralized incident-reporting and analysis system could be used by all biosafety laboratories, regardless of their containment level.

Short-term steps:

- Review current statutory or regulatory requirements for incident-reporting and determine parameters for additional reporting and analysis mechanisms, and information-sharing
- Develop a clear definition of what constitutes an incident (e.g., accident, significant exposure to a biological hazard, near miss, LAI) that should be reported
- Evaluate existing model systems for incident-reporting (e.g., the OSHA record-keeping requirements, Select Agent Program, and the incident-reporting system used by the FAA**)**
- Define the goals and key elements of a centralized system for documenting, reporting, and analyzing biosafety and biocontainment incidents that occur in high and maximum containment research facilities, and a mechanism for sharing lessons learned
- Reduce disincentives and barriers to incident-reporting at the local and national levels
- Develop incentives to induce individuals and institutions to report relevant incidents

[134] The *Select Agent Regulations* authorize the use of civil and administrative penalties in the event of non-compliance. The enabling statute authorizes criminal penalties.

Long-term steps:

- Evaluate the effectiveness of and continually improve incident-reporting, analysis, and information-sharing

Summary of Recommendation to Address Objective 4	
Objective 4	**Recommendation**
Obtain and analyze information about laboratory incidents to enable trend analysis, minimize future incidents, and share lessons learned, with the overall goals of optimizing laboratory safety and oversight.	4.1: Establish: (1) a new voluntary, non-punitive incident-reporting system for high and maximum containment research laboratories that would ensure the protection of sensitive and private information, as necessary; and (2) a centralized, integrated mechanism for analyzing incidents and sharing information and lessons learned from both current mandatory reports and the new voluntary reporting system

IX. BIOSAFETY AND BIOCONTAINMENT REGULATIONS AND GUIDELINES

OBJECTIVE 5: Ensure that biosafety and biocontainment regulations and guidelines cover current and emerging hazardous biological agents, and develop an agricultural equivalent of the *BMBL*.

Federal policies for biosafety and biocontainment oversight of high and maximum containment research need to be consistent across Federal departments and agencies. Establishing, promulgating, and updating clear biosafety and biocontainment regulations, standards, and guidelines assists scientists, research institutions, and the Federal Government in implementing comprehensive, uniform biosafety and biocontainment oversight of high and maximum containment research. Therefore, a fifth objective for improving the biosafety and biocontainment oversight framework is to ensure that biosafety and biocontainment regulations, guidelines, and oversight mechanisms cover hazardous biological agents as well as emerging technologies consistently, comprehensively, and effectively. Regulations and guidelines should be reviewed and updated at regular intervals or whenever new evidence emerges about biological agents that have the potential to pose a risk to laboratory workers, public health, agriculture, or the environment.

Currently, work performed in BSL-3, BSL-4, and equivalent agricultural containment facilities is regulated and guided by various Federal departments and agencies. The *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*), produced jointly by the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH), has become the most widely used reference in the United States for laboratory biosafety and biocontainment principles, practices, and procedures, but there is no *BMBL* equivalent for plant and livestock pathogens.[135] The *BMBL* can be useful for work with agricultural agents, but the risk assessment criteria in the *BMBL* are designed for work with pathogens and toxins that are hazardous to human health. In agricultural research laboratories, worker protection is always an important consideration. However, "…it must be noted that the risk assessment criteria for agriculture are different than those for public health and worker safety. Risk management strategies for work involving

[135] Appendix D of the *BMBL* covers the BSL-3 Ag requirements for high-consequence foreign animal diseases (i.e., those not naturally occurring in the United States and would cause significant economic impact, if introduced). For more information, see Section V and Appendix D (new in the fifth edition) of the *BMBL*, available online at http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm.

agriculture pathogens must focus on biocontainment and environmental protection in addition to worker protection, since the primary concern is the potential economic impact of the morbidity and mortality on agricultural species, and the international trade implications of a disease outbreak."[136]

The *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*) apply to any project involving recombinant DNA (rDNA) that is conducted at or sponsored by an entity that receives support for such research from the National Institutes of Health (NIH) or other Federal agencies that also require compliance with the *NIH Guidelines* as a term and condition of their grant awards. But some BSL-3 and equivalent containment research institutions do not receive funding from NIH or other Federal agencies that require compliance, and therefore are not required to adhere to the *BMBL* or the *NIH Guidelines*.

Although no Federal agency has developed comprehensive guidelines for work with all hazardous agricultural agents, some domestic and international organizations have produced guidelines to address specific needs. These include: (1) *A Practical Guide to Containment: Plant Biosafety in Research Greenhouses*, a manual that describes biological containment recommendations for plants containing rDNA (transgenic) agents or infected with plant pathogens;[137] (2) the Canadian Food Inspection Agency standards for veterinary facilities,[138] and guidelines for work with plant pests;[139] and (3) the International Biosafety Working Group guidelines on veterinary facilities. Also, Chapter 9 of the USDA Agricultural Research Service (ARS) manual 242.1(ARS Facilities Design Standard) offers guidelines for the design and construction of ARS facilities in which work with hazardous biological agents is conducted.[140]

The Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) emphasizes that whatever actions are taken to generate comprehensive guidelines for work with hazardous agricultural agents, individual protocol-driven risk assessment and risk management are paramount to ensure that research proceeds in the safest manner possible, that research is not unduly hampered, and that the United States can continue to respond quickly and effectively to agricultural and public health crises worldwide.

Issues, Options, and Recommendations to Address Objective 5

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[136] Heckert RA and Kozlovac JP. Biosafety levels for animal agriculture pathogens. *Appl. Biosafety*. 2007. 12(3): 168-173.

[137] The manual, *A Practical Guide to Containment: Plant Biosafety in Research Greenhouses*, is available at http://www.isb.vt.edu/cfdocs/greenhouse_manual.cfm.

[138] Biocontainment guidelines for veterinary facilities developed by the Canadian Food Inspection Agency are available at http://www.inspection.gc.ca/english/sci/lab/convet/convete.shtml.

[139] Biocontainment guidelines for plant pests developed by the Canadian Food Inspection Agency are available at http://www.inspection.gc.ca/english/sci/bio/plaveg/placone.shtml.

[140] The U.S. Department of Agriculture, Agricultural Research Service Manual 242.1 *ARS Facilities Design Standards*, published in 2002, is available at http://www.afm.ars.usda.gov/ppweb/PDF/242-01M.pdf.

OBJECTIVE 5 – Issue 5.1: The *BMBL* is the most widely used reference for biosafety and biocontainment principles, practices, and procedures. Additionally, Federal biosafety and biocontainment standards have been developed for research with bloodborne pathogens, select agents, agricultural agents, and rDNA. However, there currently is no agricultural equivalent to the *BMBL*.

To address this issue, the Task Force considered two options:

Option A: Develop biocontainment guidelines comparable to those of the *BMBL* (i.e., an agricultural equivalent of the *BMBL*), to cover research on plant and livestock pathogens and pests, including high and maximum containment research activities.

Option B: Expand the *BMBL* to cover research on plant and livestock pathogens and pests, including high and maximum containment research activities.

Considerations for Option A:

- Would result in similar biosafety and biocontainment standards for U.S. research activities in the agricultural sector as those for research on biological agents hazardous to human health
- Would create more comprehensive guidelines that cover all high and maximum containment research activities for research on agricultural agents
- Would need to take into account that the *BMBL* is geared primarily toward protection of laboratory workers, whereas agricultural biocontainment also is directed toward protection from environmental release of the agents under study. The *BMBL* can be useful for work with agricultural agents, but the risk assessment criteria in the *BMBL* are designed for work with pathogens and toxins that are hazardous to human health
- Would help clarify the responsibility of Federal entities by developing a separate set of agricultural guidelines

The Task Force chose not to recommend option B because entities that conduct research on hazardous agricultural agents are typically not the same as those engaged in research on agents hazardous to human health. Also, a separate set of agricultural guidelines could be updated independently of the *BMBL*. Therefore, the Task Force recommends option A because a long-standing need is for Federal biocontainment guidelines appropriate for work with agricultural pathogens and pests.

RECOMMENDATION 5.1: Develop comprehensive biocontainment guidelines comparable to those of the *BMBL* to cover research, including high and maximum containment research, on plant, livestock, and other agriculturally significant pests and pathogens.

Rationale: Developing comprehensive biosafety/biocontainment guidelines comparable to those of the *BMBL* to cover research, including high and maximum containment research, on plant, livestock, and other agriculturally significant pests and pathogens would help make biosafety and biocontainment standards for U.S. research activities in the agricultural sector more equivalent to those for research on human pathogens. In addition, it would help ensure consistency in guidelines that cover research activities in all high and maximum containment facilities, and also could help clarify the oversight responsibilities of various Federal entities.

Short-term steps:

- USDA could initiate efforts to work with Federal and non-Federal stakeholders to develop comprehensive guidelines comparable to those of the *BMBL* that describe biosafety and biocontainment principles, practices, and procedures for research with all plant, livestock, and other agriculturally significant pests and pathogens that require high or maximum containment
- Review and evaluate relevant guidelines developed by other entities for work with hazardous plant, livestock, and other significant pests and pathogens to determine whether aspects of these models could be used to establish comprehensive U.S. guidelines for work with agricultural agents

Long-term steps:

- USDA could continue to work with Federal and non-Federal stakeholders to produce and maintain comprehensive biocontainment guidelines for plant, livestock, and other significant pests and pathogens equivalent to the *BMBL*
- USDA, in collaboration with its Federal partners, could lead efforts to incorporate existing biosafety guidance and agricultural agent summary statements into appropriate existing regulatory authorities (e.g., DOL/OSHA and USDA/APHIS regulations) and requirements (e.g., *NIH Guidelines*) to include high and maximum containment research

OBJECTIVE 5 – Issue 5.2: The *Select Agent Regulations*, developed by the Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA), require compliance and include mechanisms for oversight. USDA also requires permits for the importation or interstate transfer of animals or plants if such actions are necessary to prevent the introduction into or the dissemination within the United States of pathogens or pests, and its Animal and Plant Health Inspection Service (APHIS) has the authority to inspect facilities that possess or use plants, animals, or other biological agents and products (viruses, toxins, and sera) covered by the USDA regulations. Occupational Safety and Health Administration (OSHA) regulations (*General Duty Clause, Personal Protective Equipment Standards, Bloodborne Pathogens Standard*, *Respiratory Protection Standard*, and *Hazard Communication Standard*) apply to all workplaces. Federal regulations pertaining to work with the most hazardous

biological agents require local and Federal biosafety and biocontainment oversight. Already in place are mechanisms to review and update biosafety and biocontainment regulations, guidelines, and associated oversight mechanisms. (See Chapter III for more information on biosafety and biocontainment regulations and guidelines.)

However, there is no Federal requirement for institutional or Federal biosafety and biocontainment oversight of research involving a small number of other hazardous, non-recombinant biological agents such as hantavirus, SARS, and extensively drug-resistant *M. tuberculosis* that are studied in BSL-3 facilities. (Research in BSL-4 and equivalent containment facilities is covered by existing regulations because these entities possess, use, or transfer select agents or toxins.) Also, biosafety and biocontainment regulations and oversight mechanisms need to keep pace with research on new and emerging technologies and research needs (e.g., work with synthetic agents such as those produced through nanotechnology, certain genetic elements, and even whole genomes of many highly pathogenic organisms, when chemically synthesized from nucleotides).[141]

Biosafety and biocontainment regulations, guidelines, and oversight mechanisms have been developed on the basis of information currently available. Because new infectious agents continue to emerge and re-emerge, and the fields of biotechnology and synthetic biology are advancing rapidly, associated biosafety and biocontainment regulations, guidelines, and oversight mechanisms need to be updated on a regular basis and as necessary.

Efforts to develop the current versions of the *Select Agent Regulations* and the *BMBL* were collaborative, and involved key Federal and non-Federal stakeholders with expertise in many disciplines. It is important to ensure that continued broad-based participation by all relevant stakeholders occurs.

The Task Force discussed the importance of rigorous and comprehensive processes for the review and updating of biosafety and biocontainment regulations, guidelines, and associated oversight mechanisms. These processes must ensure that all high and maximum containment research activities and facilities are appropriately covered; that reviewing and updating biosafety/biocontainment regulations, guidelines, and associated oversight mechanisms occurs periodically and as needed; and that the processes continue to include collaboration with and broad-based participation by all relevant stakeholders.

Considerations:

- Would ensure that biosafety and biocontainment regulations and guidelines provide comprehensive coverage of research on potentially

[141] NIH proposed broadening the scope of the *NIH Guidelines* to encompass work with nucleic acids (both DNA and RNA) that are synthesized chemically without the use of recombinant technology, and to address the biosafety principles and practices applicable to work with synthetic nucleic acids. This change reflects the fact that traditional rDNA techniques are no longer the only way to create new nucleic acid structures and that it is the use of the novel nucleic acid product—and not the technology used to create that product—that needs to be subject to biosafety oversight. The proposed change was published in the Federal Register. (See 74 Fed. Reg. 9411 [March 4, 2009].)

hazardous biological agents at all high and maximum containment facilities in all sectors (i.e., in all relevant government, academic, commercial, and private research facilities)
- Would ensure that biosafety/biocontainment regulations and guidelines keep pace with progress in science (e.g., with emerging technologies)
- Would involve subject-matter experts in the continual review of biosafety/biocontainment regulations and guidelines

The Task Force considered it essential to ensure that all potentially hazardous biological agents are addressed by biosafety/biocontainment regulations and guidelines, that the review of biosafety/biocontainment regulations and guidelines occurs on a periodic basis, and that these processes include broad-based participation by all relevant stakeholders.

RECOMMENDATION 5.2: Maintain rigorous and comprehensive processes for the review and updating of biosafety and biocontainment regulations and guidelines, and ensure that these processes include broad-based participation by all relevant stakeholders.

Rationale: It is necessary to maintain rigorous and comprehensive processes to ensure that Federal regulations, guidelines, and associated oversight mechanisms are timely and sufficiently comprehensive. These processes should utilize, and expand upon, as appropriate, existing mechanisms for the review and updating of biosafety regulations and guidelines, and should include broad-based participation by all relevant stakeholders. If deemed appropriate, a new Federal entity for coordinating biosafety and biocontainment oversight (as proposed in Recommendation 1.1) could ensure timely, comprehensive revisions of biosafety and biocontainment regulations and guidelines.

Short-term steps:
- Evaluate and determine whether Federal regulations and guidelines and their statutory basis are sufficiently comprehensive
- Determine what additions or improvements to Federal biosafety and biocontainment regulations and guidelines or the underlying statutory authorities might be necessary

Long-term steps:
- If needed, develop and implement improved Federal biosafety and biocontainment regulations and guidelines
- Engage Federal and non-Federal stakeholders, including professional organizations (e.g., the American Society of Microbiology (ASM) and the American Biological Safety Association (ABSA)) to develop mechanisms to ensure for biosafety/biocontainment regulations, guidelines, and oversight mechanisms are up to date

Summary of Recommendations to Address Objective 5	
Objective 5	**Recommendations**
Ensure that biosafety and biocontainment regulations and guidelines cover current and emerging hazardous biological agents, and develop an agricultural equivalent of the *BMBL*.	5.1: Develop comprehensive biocontainment guidelines comparable to those of the *BMBL* to cover research, including high and maximum containment research, on plant, livestock, and other agriculturally significant pests and pathogens.
	5.2: Maintain rigorous and comprehensive processes for the review and updating of biosafety and biocontainment regulations and guidelines, and ensure that these processes include broad-based participation by all relevant stakeholders.

X. INFRASTRUCTURE MAINTENANCE AND SHARING BEST PRACTICES

OBJECTIVE 6: Ensure that the infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained.

Effective biosafety and biocontainment oversight is dependent on ensuring that the infrastructure and equipment of these facilities are appropriately maintained, and that facility operations, in addition to actual laboratory operations, at all high and maximum containment research facilities in all sectors are safe. BSL-3, BSL-4, and equivalent agricultural containment facilities are designed to house the most hazardous microorganisms and biological toxins, and to contain the release of any biohazardous aerosols, liquids, or solids. Any mechanical failure of key facility systems or minor structural defects—such as cracks in a wall or leaky pipes—could have severe consequences. For that reason, the physical containment structure and supporting infrastructure, including heat and air-conditioning systems, back-up power, plumbing and waste-treatment systems, must be secure and well-maintained.

Significant resources have been invested in the construction of new high and maximum containment research facilities and the equipment necessary for biosafety and biocontainment. It is equally important to ensure adequate resources are available for their operation and maintenance. Typically, for laboratory construction projects, funding comes from defined resources dedicated to design, construction, and initial commissioning. In contrast, resources for ongoing operations and safety maintenance typically are derived from chargeback or overhead fees deducted as a facility- or agency-specified percentage from grants or other research budgets. Ideally, funding for facility infrastructure maintenance and operations should be separate from the resources provided for research activities.

Issues and Options to Address Objective 6

OBJECTIVE 6 − Issue 6.1: There currently is no formal mechanism to ensure the infrastructure and equipment necessary for biosafety and biocontainment at all high and maximum containment research facilities are adequately maintained, or that the operations of these facilities are safe. Also, there is no mechanism to ensure adequate resources are available for these activities.

To address this issue, the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) discussed the need for establishing

mechanisms to ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment at all high and maximum containment research laboratories in all sectors.

Considerations:

- Would require a comprehensive review of existing mechanisms and resources at high and maximum containment research facilities for infrastructure maintenance and safety of operations
- Would help ensure more effective and consistent maintenance of physical containment structure and supporting infrastructure at high and maximum containment research facilities
- Would help ensure that facility operations, in addition to laboratory operations, are safe
- Would help promote public confidence and trust that institutional oversight mechanisms are consistent and effective
- Would require a determination of what additional strategies are needed to support facility operations and safety maintenance costs without drawing from research funds

The Task Force appreciates that many, if not most, high and maximum containment research facilities currently are adequately maintained and safely operated, but concluded it is important to ensure that *all* these facilities are adequately maintained and safely operated now and in the future.

RECOMMENDATION 6.1: Require that all institutions with high or maximum containment laboratories ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment.

Rationale: Achieving safe operation and effective oversight of all high and maximum containment research facilities in all sectors requires that infrastructure (e.g., for the physical containment structure, heating and air conditioning, back-up power, plumbing, and waste-treatment systems) be installed properly and sufficiently and routinely maintained. Also, infrastructure should be repaired and upgraded, as necessary, and all operations of these facilities should occur using appropriate safety and containment practices. Achieving these goals will require: (1) proper installation of equipment; (2) a clear process for continual safety maintenance, as well as safety procedures and protocols for off-cycle or unplanned repairs; (3) a designated person(s) who is experienced in safely operating and maintaining critical equipment and who could advise the senior institutional official (described in Recommendation 1.3), and act as a point of contact for regulatory and funding agencies regarding the operation and maintenance of the facility; and (3) a dedicated operating budget for safety maintenance and facility operations.

Short-term steps:

- Appoint a task force comprised of representatives from Federal agencies and other stakeholders to:
  - Review and determine the adequacy of current mechanisms for ensuring the proper installation and necessary maintenance, repair, and upgrades of facility infrastructure, and the safety of operations at all high and maximum containment research laboratories in all sectors
  - Review the feasibility of creating a Federal program to support major infrastructure repair and upgrades for Federally owned (e.g., by the Departments of Agriculture [USDA], Health and Human Services [HHS], Homeland Security [DHS], Energy [DOE], and Defense [DOD]), the Environmental Protection Agency (EPA), and Federally funded high and maximum containment research facilities (including the National and Regional Biocontainment Laboratories [NBLs and RBLs]),[142] and the new National Bio and Agro-Defense Facility (NBAF), which will be designed for research on high-consequence zoonotic agents and foreign animal diseases.[143])

Long-term steps:

- Determine whether imposing this new requirement that high and maximum containment research institutions ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment requires new statutory and/or regulatory authority
- Require all high and maximum containment research facilities in all sectors to implement mechanisms for appropriate infrastructure installation, maintenance, repair, and upgrades, and for ensuring the safety of operations
- Require all high and maximum containment research facilities in all sectors to:
  - Develop a safety maintenance master plan to include mechanisms for continual safety maintenance, safety procedures and protocols for off-cycle or unplanned repairs, identifying safety maintenance issues, methods to determine the priority of each issue (to help establish the budget), and criteria for determining when equipment (or the entire facility) needs to be replaced
  - Designate a person(s) knowledgeable about and responsible for infrastructure and equipment installation, and safety maintenance who could advise the senior institutional official (described in Recommendation 1.3), and act as a point of contact for regulatory and

[142] For more information on National and Regional Biocontainment Laboratories (NBLs and RBLs), see http://www3.niaid.nih.gov/research/resources/dmid/NBL_RBL/. The National Institute of Allergy and Infectious Diseases (NAID) funds the construction of NBLs and RBLs.

[143] For more information on the National Bio and Agro-Defense Facility (NBAF), see http://www.dhs.gov/xres/labs/editorial_0762.shtm. DHS has overall responsibility for NBAF.

funding agencies regarding infrastructure and equipment installation, and the operation and maintenance of the facility

- If identified as feasible, develop and implement a Federal program to fund major infrastructure repair and upgrades for Federally owned and Federally supported high and maximum containment research facilities

OBJECTIVE 6 − Issue 6.2: Currently, there are no comprehensive Federal guidelines or best practices for infrastructure and equipment design, operations, and safety maintenance at high and maximum biosafety and biocontainment facilities in all sectors.[144] Instead, individuals at each institution are responsible for identifying, developing, and optimizing their own practices and procedures for infrastructure maintenance and facility operations.

To address this issue, the Task Force discussed how best to communicate information about best practices among high and maximum containment research facilities in all sectors, with the goals of identifying trends and sharing lessons learned about infrastructure and equipment design, operations, and maintenance.

Considerations:

- Would help disseminate information about best practices, infrastructure and equipment design, operations, maintenance, and ways to enhance the overall safety and oversight of high and maximum containment research facilities
- Could provide a means to identify trends, shared problems, and lessons learned about infrastructure and equipment design, operations, and maintenance in high and maximum containment research facilities, and help determine whether further Federal guidance, funding, or research is necessary to resolve these issues
- Could require that an entity (perhaps the centralized Federal entity described in Recommendation 1.1) establishes an information clearinghouse for identifying and sharing best practices among U.S. high and maximum containment research facilities
- Would establish a means to provide formal assurance that institutions with high and maximum containment research facilities are complying with best practices for infrastructure and equipment design, operations, and maintenance

The Task Force also considered and rejected the possibility of not exploring mechanisms by which high and maximum containment research facilities in the United States could share information about best practices, infrastructure and equipment design, operations, and maintenance, i.e., of maintaining the *status quo*. Every effort must be made to ensure

[144] The widely used guidance document, *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*), emphasizes the need for routine inspection, testing, and maintenance of biosafety cabinets, but does not address maintenance issues or best practices that pertain to supporting infrastructure such as heat and air-conditioning systems, back-up power, or plumbing and waste-treatment systems.

that these facilities and equipment are installed properly, maintained effectively, and operated safely. (For information about facility inspections, see Appendix J.)

RECOMMENDATION 6.2: Develop a mechanism for sharing information and best practices about infrastructure and equipment design, operations, and maintenance among all high and maximum containment research facilities.

Rationale: High and maximum containment research facilities, although designed for specific purposes, nevertheless have in common a range of safety features, operations, and maintenance practices. A mechanism to identify and share best practices about infrastructure and equipment design, operations, and maintenance would likely enhance overall biosafety and biocontainment and facilitate oversight of these activities.

Short-term steps:

- Identify best practices for infrastructure and equipment design, operations, and maintenance at high and maximum containment research laboratories
- Establish a mechanism to share best practices, identify trends or problems, and share lessons learned among high and maximum containment research facilities, perhaps by tasking the centralized Federal entity described in Recommendation 1.1 to develop an information clearinghouse
- Conduct a review to determine whether new statutory and/or regulatory authority is required to share or disclose such information

Long-term steps:

- Include information about best practices for infrastructure and equipment design, operations, and maintenance of high and maximum containment research laboratories in relevant Federal regulations and guidelines

Summary of Recommendations to Address Objective 6	
Objective 6	**Recommendations**
Ensure that the infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained.	6.1: Require that all institutions with high or maximum containment laboratories ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment.

	6.2: Develop a mechanism for sharing information and best practices about infrastructure and equipment design, operations, and maintenance among all high and maximum containment research facilities.

XI. BIOSAFETY AND BIOCONTAINMENT RESEARCH PROGRAMS

OBJECTIVE 7: Develop and support a national research agenda for applied biosafety and biocontainment to improve the management of biohazard risks.

A seventh objective is to develop and support a national research agenda for applied biosafety research, thereby ensuring the development of new, science-based biosafety and biocontainment practices, improved equipment and technology, risk-assessment methodologies, and procedures to manage biohazard risks.

Funding for applied biosafety and biocontainment research has decreased markedly since the 1980s. The practices and procedures—e.g., for performance-testing, disinfection, decontamination, and sterilization—engineering controls, and personal protective equipment currently used in high and maximum containment research laboratories are based in large part on the results of studies performed decades ago. Today, there are extremely limited resources directed toward developing new, scientifically based information about biosafety and biocontainment practices and procedures, engineering controls, and risk-assessment methodology. Support for this much-needed area of research will yield evidence-based improvements in biosafety and biocontainment practices, procedures, engineering controls, protective equipment, and facility design that will enhance the safety of biological laboratories, including BSL-3, BSL-4, and equivalent agricultural containment research facilities. There was considerable and widespread support from key stakeholders and the public for the provision of increased resources for this critical area of applied biosafety and biocontainment research, based upon input received during the public meeting held December 8-9, 2008.

Issues, Options, and Recommendations to Address Objective 7

OBJECTIVE 7 − Issue 7.1: Applied biosafety and biocontainment research programs are needed to further develop science-based practices and procedures, engineering controls, personal protective equipment, and risk-assessment methodologies necessary to optimize the safety of BSL-3, BSL-4, and equivalent agricultural containment research facilities; and to keep safety equipment, practices, and procedures up to date.

The Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) discussed the need to develop and maintain a robust program of applied biosafety and biocontainment research to create additional and update existing evidence-based practices and technologies to improve the management of biohazard risks.

Considerations:

- Would generate additional science-based practices and procedures, decontamination methodologies, engineering controls, and protective equipment that could better protect laboratory personnel, public health, agriculture, and the environment
- Would generate evidence-based improvements in risk assessment and risk-management methodologies for use by researchers, biosafety professionals, and institutional biosafety review committees
- Would help improve biosafety and biocontainment in all biological laboratories, including BSL-3, BSL-4, and equivalent agricultural containment research facilities
- Would stimulate universities and other entities to become involved in applied biosafety and biocontainment research
- Would need to be based on peer-reviewed, meritorious science

The Task Force considered the possibility of maintaining the *status quo*. However, the need to enhance the evidence base for biosafety and biocontainment equipment and practices through the development of applied research programs on these topics is underscored by the recent increase in the number of high and maximum biocontainment laboratories. Therefore, critical to optimizing biosafety and biocontainment practices and procedures, decontamination methodologies, engineering controls, and protective equipment is the development and support of a robust applied biosafety research program.

RECOMMENDATION 7.1: Develop and maintain a robust program of applied biosafety and biocontainment research to create additional and update existing evidence-based practices and technologies.

Rationale: A robust program of applied biosafety and biocontainment research is necessary for the development of new, evidence-based biosafety and biocontainment practices, improved equipment/technology, risk-assessment methodologies, and procedures to manage biohazard risks.

Short-term steps:

- Engage Federal and non-Federal stakeholders to determine priorities in applied biosafety and biocontainment research
- Develop mechanisms to encourage a robust applied biosafety and biocontainment research program to continue developing new, science-based biosafety and biocontainment practices, improved equipment/technology, risk assessment methodologies, and procedures to manage biohazard risks

Long-term steps:

- Stimulate applied biosafety and biocontainment research that will lead to increased knowledge and improvements in biosafety and biocontainment practices
    - Generate new and improved biosafety/biocontainment practices and procedures, performance testing, decontamination methodologies, engineering controls, and protective equipment that could better protect laboratory personnel, public health, agriculture, and the environment
    - Improve risk assessment and risk-management methodologies for use by researchers, biosafety professionals, and institutional biosafety review committees

Summary of Recommendation to Address Objective 7	
Objective 7	**Recommendation**
Develop and support a national research agenda for applied biosafety and biocontainment to improve the management of biohazard risks.	7.1: Develop and maintain a robust program of applied biosafety and biocontainment research to create additional and update existing evidence-based practices and technologies.

XII. PUBLIC COMMUNICATION, OUTREACH, AND TRANSPARENCY

OBJECTIVE 8: Improve and share strategies to ensure effective public communication, outreach, and transparency about biosafety and biocontainment issues.

A final objective identified by the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force) is to improve, where necessary, mechanisms to promote public communication, outreach, and transparency about many aspects of high and maximum containment research, including safety, containment procedures and equipment, and oversight. Also important is the need to coordinate messages about common biosafety/biocontainment themes and topics. Although many Federal agencies and non-Federal entities have developed public education and outreach programs for stakeholders, including individuals who work in, oversee, support, or manage research laboratories (see Appendix F), there is no formalized system for educating the general public about the need for high and maximum containment research laboratories, or decisions about the expansion, construction, and placement of these facilities. Additionally, there is no formalized, broadly applied mechanism outside the process defined in the National Environmental Policy Act and its implementing regulations that allows the Federal Government to address potential public concerns about the functions and activities of these facilities, once built.

Issues, Options, and Recommendations to Address Objective 8

OBJECTIVE 8 − Issue 8.1: There is a need for improved public communication, outreach, and transparency about biosafety and biocontainment issues, and high and maximum containment research facilities and activities.

The Task Force discussed the importance of improving public communication, outreach, and transparency about biosafety and biocontainment issues, and high and maximum containment research facilities and activities.

Considerations:

- Would increase the quality and quantity of information exchanged between the public and the scientific community
- Could help enhance public trust in the research enterprise, and help cultivate public support for research on hazardous biological agents
- Would enhance the dissemination of information about the mechanisms in place to ensure the safety of laboratory personnel, the public, agriculture, and the environment
- Would help provide mechanisms to:

- Communicate proposed changes to the biosafety and biocontainment oversight framework
- Share information about incidents at high and maximum containment research facilities

RECOMMENDATION 8.1: Develop comprehensive strategies to improve public communication, outreach, and transparency about biosafety and biocontainment issues and activities at high and maximum containment research facilities.

Rationale: Public communication, outreach, and transparency are shared responsibilities between the Federal Government and individual research institutions. Key to the success and acceptance of research in high and maximum containment facilities are effective mechanisms for public communication, outreach, and transparency about many aspects of the research facilities and their operations, including safety, containment procedures and equipment, and oversight. Additionally, messages should be developed that articulate the need for expanding the capacity of such research activities and the associated infrastructure.

Short-term steps:

- Identify and share principles and practices that have proven effective to improve public communication, outreach, and transparency
- With consideration of community interests in mind, develop a comprehensive strategy for mechanisms to ensure public transparency without jeopardizing security, or proprietary or private information
- Explore and identify strategies best suited to understand and respond to public questions and comments

Long-term steps:

- Establish a comprehensive strategy to ensure effective and consistent communications strategies that can be shared between the Federal Government and individual research institutions
- Develop mechanisms to evaluate on a continuing basis the effectiveness of efforts to improve public communication, outreach, and transparency

Summary of Recommendation to Address Objective 8	
Objective 8	**Recommendation**
Improve and share strategies to ensure effective public communication, outreach, and transparency about biosafety and biocontainment issues.	8.1: Develop comprehensive strategies to improve public communication, outreach, and transparency about biosafety and biocontainment issues and activities at high and maximum containment research facilities.

XIII. SUMMARY OF TASK FORCE RECOMMENDATIONS FOR OPTIMIZING BIOSAFETY AND BIOCONTAINMENT OVERSIGHT

The following table summarizes the objectives and recommendations of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force). In some cases, implementing these recommendations will require the addition or redirection of resources. Also, the Task Force recognizes that legislation or rulemaking will be required to implement the recommendations in all sectors.

Summary of Objectives and Recommendations

Objectives	Recommendations
1. Enhance the overarching framework for biosafety and biocontainment oversight of high and maximum containment research through improved coordination of oversight activities.	1.1: Identify or establish a Federal entity to coordinate biosafety and biocontainment oversight activities, and to ensure comprehensive and effective Federal oversight for all high and maximum containment research facilities and activities in all sectors.
	1.2: Develop a registry of all high and maximum containment facilities in the United States.
	1.3: Require that all institutions conducting high and maximum containment research designate: (1) a senior official with the appropriate knowledge, authority, and accountability who is responsible for institutional compliance with biosafety and biocontainment regulations and guidelines; (2) a credentialed biosafety professional (see Recommendation 3.3) who is responsible for oversight of biosafety and biocontainment programs.
	1.4: Require that, at all institutions conducting high or maximum containment research, an appropriately constituted review body performs a thorough risk assessment of all laboratory protocols potentially requiring high or maximum containment.
2. Encourage a robust culture of accountability characterized by individual and institutional compliance with biosafety and biocontainment regulations, guidelines, standards, and policies.	2.1: Mandate compliance with Federal biosafety and biocontainment guidelines, including the *BMBL* and the *NIH Guidelines*, for all high and maximum containment research institutions in all sectors.
	2.2: Support the development of an accreditation system for biosafety/biocontainment management programs at high and maximum containment research institutions.
3. Develop a national strategy to enable and ensure the appropriate training and technical competence of all individuals who work in, oversee, support, or manage high or maximum containment research laboratories.	3.1: Establish national, position-specific training standards and core competencies in biosafety and biocontainment for all research, managerial, and support personnel at high and maximum containment research laboratories in all sectors.
	3.2: Require institutions to ensure that all individuals who work in, oversee, support, or manage high or maximum containment research laboratories are appropriately trained and competent in biosafety and biocontainment.
	3.3: Implement a phased-in requirement that the designated biosafety professional (Biological Safety Officer or equivalent) at

	all high and maximum containment research facilities be credentialed.
4. Obtain and analyze information about laboratory incidents to enable trend analysis, minimize future incidents, and share lessons learned, with the overall goals of optimizing laboratory safety and oversight.	4.1: Establish: (1) a new voluntary, non-punitive incident-reporting system for high and maximum containment research laboratories that would ensure the protection of sensitive and private information, as necessary; and (2) a centralized, integrated mechanism for analyzing incidents and sharing information and lessons learned from both current mandatory reports and the new voluntary reporting system.
5. Ensure that biosafety and biocontainment regulations and guidelines cover current and emerging hazardous biological agents, and develop an agricultural equivalent of the *BMBL*.	5.1: Develop comprehensive biocontainment guidelines comparable to those of the *BMBL* to cover research, including high and maximum containment research, on plant, livestock, and other agriculturally significant pests and pathogens.
	5.2: Maintain rigorous and comprehensive processes for the review and updating of biosafety and biocontainment regulations and guidelines, and ensure that these processes include broad-based participation by all relevant stakeholders.
6. Ensure that the infrastructure and equipment necessary for biosafety and biocontainment at high and maximum containment research facilities are in place and properly maintained.	6.1: Require that all institutions with high or maximum containment laboratories ensure proper installation of and preventive and ongoing maintenance programs for biosafety and biocontainment infrastructure and equipment.
	6.2: Develop a mechanism for sharing information and best practices about infrastructure and equipment design, operations, and maintenance among all high and maximum containment research facilities.
7. Develop and support a national research agenda for applied biosafety and biocontainment to improve the management of biohazard risks.	7.1: Develop and maintain a robust program of applied biosafety and biocontainment research to create additional and update existing evidence-based practices and technologies.
8. Improve and share strategies to ensure effective public communication, outreach, and transparency about biosafety and biocontainment issues.	8.1: Develop comprehensive strategies to improve public communication, outreach, and transparency about biosafety and biocontainment issues and activities at high and maximum containment research facilities.

Conclusion

A robust system for biosafety and biocontainment oversight of high and maximum containment research and related activities is in place. The objectives and recommendations in this report are designed to optimize local biosafety and biocontainment oversight at individual high and maximum containment research facilities; improve and better coordinate Federal oversight of these facilities and their activities; and help increase public confidence and trust that high and maximum containment research laboratories in the United States are being operated as safely as possible.

Report of the Trans-Federal Task Force on
Optimizing Biosafety and Biocontainment Oversight

Glossary

Accreditation – For the purposes of this report, the term accreditation refers to an objective assessment of an institution's biosafety/biocontainment or biorisk management program by an independent body. Accreditation would allow the institution to demonstrate that its biosafety and biocontainment programs meet or exceed national standards. This approach is comparable to the CEN laboratory biorisk management standard,[145] which indicates "… a biohazard, or biorisk management program is that part of an organization's management system used to develop and implement its policy established to manage its biohazards. A management system approach to biohazard risks implies that identifying, understanding and managing a system of interrelated processes for a given objective, improves the organization's effectiveness and efficiency."

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

Animal biosafety levels (ABSL) – Designations of laboratories in ascending order based on the degree of risk associated with the work being conducted. The designations ABSL-1, ABSL-2, ABSL-3, ABSL-3 "enhanced,"[146] and ABSL-4[147] are for work with biohazards used in a vivarium that include zoonotic or human pathogens.

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

Biocontainment – A term used differently in facilities for the study of human pathogens versus those used for the study of agricultural pathogens. *1. In agricultural facilities*, the definition for "biocontainment" resembles that for "biosafety," i.e., the safety practices and procedures used to prevent unintended infection of plants or animals or the release of high-consequence pathogenic agents into the environment (air, soil, or water). *2. However, for all high and maximum containment facilities*, "biocontainment" also refers

[145] CEN is the European Committee for Standardization (Comité Européen de Normalisation). The February 2008 version of the CEN document, entitled *Laboratory Biorisk Management Standard* (CWA 15793) is available at http://www.cen.eu/CENORM/Sectors/technicalcommitteesworkshops/workshops/ws31.asp.

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

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

to the physical containment barriers in a facility such as contained dressing and shower rooms, sealed service penetrations, specialized doors, entry and exit avenues to prevent cross-contamination, specialized air handling systems for contamination control, personal protective equipment, biosafety cabinets, etc.

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

Biological agent – Any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment. (From the CDC Select Agents and Toxins Final Rule. 72 CFR 73.1 Definitions).[148]

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

Biosafety – The application of combinations of laboratory practices and procedures, laboratory facilities, safety equipment, and appropriate occupational health programs when working with potentially infectious microorganisms and other biohazards.[149] Biosafety practices and procedures are designed to reduce the exposure of laboratory personnel, the public, agriculture, and the environment to potentially infectious agents and other biological hazards. The key principles of biosafety are risk assessment and containment. The principles of biosafety have been articulated in two key reference documents, the *NIH Guidelines for Research Involving Recombinant DNA Molecules*[150] (first published in 1976), and the manual titled *Biosafety in Microbiological and Biomedical Laboratories*[151] *(BMBL*, initially issued in 1984). These documents have both been amended and revised over the years to reflect advances in science and technology.

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[148] The 2005 final *Select Agent Regulations* are available at http://www.selectagents.gov/selagentRegulation.htm.
[149] Definition adapted from CDC definition available at http://www.cdc.gov/od/ohs/pdffiles/Module%202%20-%20Biosafety.pdf.
[150] The *NIH Guidelines* are available at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.
[151] For the online fifth edition of the *BMBL*, see http://www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm.

For more than two decades, the *BMBL* has been the code of practice for biosafety in the United States.

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

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

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

Biosafety officer (biological safety officer or BSO) – An individual who acts as a technical resource to scientific and management staff by assisting in the conduct of risk assessments and risk management involving work with biological hazards including recombinant DNA. BSOs promote compliance with biosafety and biocontainment regulations, guidelines, and policies in each laboratory, and assist in the development of emergency response plans. This position and its suggested function(s) are described in several documents such as the *NIH Guidelines*, WHO *Laboratory Biosafety Manual*, Third Edition, and the Army Pamphlet (DA PAM) 385-69.[152]

Biosafety professional – The term used in this report to indicate a professional highly trained in biosafety and biocontainment principles and practices (e.g., a BSO or

[152] *The NIH Guidelines* (Section IV-B-3) are available at http://oba.od.nih.gov/oba/index.html; the Army, DA PAM 385-69 (section 3-3) is available at http://www.apd.army.mil/usapa_home.asp; and the WHO *Laboratory Biosafety Manual*, Third Edition, is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf.

equivalent) who promotes safe laboratory practices, procedures, and proper use of containment equipment and facilities; stimulates responsible activities among workers; and provides advice on laboratory design. Regardless of their initial training (e.g., as microbiologists, biologists, molecular biologists, environmental health professionals, industrial hygienists, clinical health care professionals, veterinarians, and engineers), biosafety professionals must develop knowledge of the principles of epidemiology, disease transmission patterns, risk-assessment/ risk management methodology, disinfection and sterilization techniques, disease prevention, aerobiology, and environmental control. Biosafety professionals work in concert with other laboratory personnel who handle pathogenic or potentially infectious microorganisms, recombinant DNA molecules and organisms containing them, and biological toxins.[153] They typically serve on biosafety review committees, and are involved in the development and implementation of institutional biosafety/biocontainment management programs. Ideally, biosafety professionals, BSOs, and their equivalents should be credentialed (registered or certified) by a responsible entity.

Biosafety review committee –The term used in this report to refer to a group of individuals affiliated with a facility whose functions typically extend beyond those of the "institutional biosafety committee" (IBC) as described in the *NIH Guidelines*. Suggested functions for a biosafety review committee also are described in other documents including the WHO *Laboratory Biosafety Manual*, Third Edition, and the Army biosafety pamphlet DA PAM 385-69. Common roles of a biosafety committee include participation in development of institutional biosafety policies and codes of practice and Risk assessments based on reviews of laboratory protocols for work involving hazardous biological agents, recombinant DNA other genetically modified materials, and potentially hazardous synthetic agents. Other functions of the committee may include the formulation of new safety policies and arbitration in disputes over safety matters.[154]

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

Certification – A term used differently in different contexts to refer to the process of validating the expertise and credentials of an individual or an engineering control and in some cases a laboratory facility. *1. For an individual*, "certification" refers to a valuable step in professional development. Individuals pursuing certification must demonstrate they meet established educational criteria, and must also meet the prerequisite experience relevant to the area in which certification is being sought. Relevant experience is experience in which a significant majority of the candidate's duties is in the area in which he/she is seeking certification. After the certifying body has verified, through a review of relevant documents, that the individual has met both requirements, the individual will be

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

[154] *The NIH Guidelines* are available at http://oba.od.nih.gov/oba/index.html; the Army DA PAM 385-69 is available at http://www.apd.army.mil/usapa_home.asp; and the WHO *Laboratory Biosafety Manual*, Third Edition, is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf.

eligible to sit for a certification exam, which will test their knowledge in the area they are seeking certification. *2. For an engineering control* which, in many cases will have two distinct types of certification; i.e., biological safety cabinets (BSC) have design certification to a standard and a field operation standard. BSC design certification is formal validation by a qualified design testing organization that a designated cabinet model meets all the requirements of National Sanitation Foundation (NSF) Standard 49, annex A; whereas BSC Field Certification is formal verification by a qualified field testing certifier that an installed cabinet meets all the requirements of NSF Standard 49, annex F of this standard. *3. For a facility*, the term "certification" is not widely used, and is not based upon an internationally recognized standard (e.g., as is the case for BSC design, per NSF 49). For the purposes of this report, facility certification refers only to the National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements, which describes the systematic review of all safety features and processes associated with the laboratory (engineering controls, personal protective equipment, building and system integrity, standard operating procedures [SOPs] and administrative controls, such as documentation and record retention systems).[155] This validation assures that all reasonable facility controls and prudent practices are in place to minimize, to the greatest extent possible, the risks associated with laboratory operations and the use of biohazardous materials.

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

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

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

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

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

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[155] Definition adapted from the "National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements," available at http://dohs.ors.od.nih.gov/pdf/BSL3%20CertificationRequirements-FINAL.pdf. NIH uses the term "certification" to refer to a laboratory, whereas other entities typically refer to "accreditation" of a facility.

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

Incident − For the purposes of this report, a laboratory event that may include exposure of staff or the public to an infectious, potentially infectious, or zoonotic agent; environmental release of a biological hazard; escape of infected animals or vectors; spill of a biohazard outside of a primary containment device; loss or theft of biohazardous agents and other loss of containment; or equipment failure in conjunction with a biohazard (e.g., centrifuge accident) that may lead to a release of a hazardous agent within the laboratory environment or outside the laboratory environment. An incident or accident can cause a laboratory-acquired illness (LAI).[156]

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

Institutional biosafety committee (IBC) – A committee comprised of no fewer than five members so selected that they collectively have experience and expertise in recombinant DNA technology and the capability to assess the safety of recombinant DNA research and to identify any potential risk to public health or the environment.[157]

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

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

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

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

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

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

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

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

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

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

Regulation – A rule based on a statute. *1.* For the purposes of this report, a Federal regulation is a statement by a Federal agency[158] designed to implement, interpret, or prescribe law or policy or describing the organization, procedure, or practice requirements of an agency promulgated in accordance with the *Administrative Procedure Act*. Once adopted, a Federal regulation is legally binding. The *Select Agent Regulations* are an example of biosafety and biosecurity regulations. *2.* State and local regulations are administrative rules or directives developed by State and local officials in addition to Federal regulations. Once adopted, a State or local regulation is legally binding.

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

Risk assessment – A process used to identify the hazardous characteristics of a known infectious agent or potentially infectious agent or material, the activities that can result in exposure to such an agent, the likelihood that such exposure will cause a laboratory-acquired infection (LAI), and the probable consequences of such an infection. The key principle in selecting the appropriate safeguards for the conduct of the microbiological research or work at hand is "risk assessment." The information identified through risk assessment is used to guide the selection of appropriate microbiological practices, safety equipment, and facility safeguards that, when used properly, can prevent exposures and

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

dramatically reduce the incidence of LAIs. Risk assessment is a common first step in an overall risk-management process. This approach has been used successfully for decades to allow the safe conduct of microbiological research and manipulation of clinical microbiological specimens. (Adapted from the *BMBL*)

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

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

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

Weapons of Mass Destruction (WMD) – Nuclear, biological, and chemical devices that can cause destruction on a vastly greater scale than any conventional weapons. (Adapted from the report, *Weapons of Terror*, available at http://www.wmdcommission.org/)

LISTS OF HHS AND USDA SELECT AGENTS AND TOXINS
(7 CFR 331, 9 CFR 121, and 42 CFR 73)

HHS/CDC Select Agents and Toxins
(9 CFR 121.3)

Abrin
Botulinum neurotoxins
Botulinum neurotoxin-producing species of *Clostridium*
Cercopithecine herpesvirus 1 (Herpes B virus)
Clostridium perfringens epsilon toxin
Coccidioides posadasii/Coccidioides immitis
Conotoxins
Coxiella burnetii
Crimean-Congo haemorrhagic fever virus
Diacetoxyscirpenol
Eastern Equine Encephalitis virus
Ebola viruses
Francisella tularensis
Lassa fever virus
Marburg virus
Monkeypox virus
Reconstructed replication-competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 influenza virus)
Ricin
Rickettsia prowazekii
Rickettsia rickettsii
Shigatoxin
Saxitoxin
Shiga-like ribosome inactivating proteins
South American Haemorrhagic Fever viruses (Flexal, Guanarito, Junin, Machupo, Sabia)
Staphylococcal enterotoxins
T–2 toxin
Tetrodotoxin
Tick-borne encephalitis complex (flavi) viruses
- Central European Tick-borne encephalitis
- Far Eastern Tick-borne encephalitis
- Russian Spring and Summer encephalitis
- Kyasanur Forest disease
- Omsk Hemorrhagic Fever

Variola major virus (Smallpox virus)
Variola minor virus (Alastrim)
Yersinia pestis

HHS and USDA Overlap Select Agents and Toxins
(42 CFR 73.4 and 9 CFR 121.4)

Bacillus anthracis
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei*)
Burkholderia pseudomallei (formerly *Pseudomonas pseudomallei*)
Hendra virus
Nipah virus
Rift Valley fever virus
Venezuelan Equine Encephalitis virus

USDA/APHIS Select Agents and Toxins
(9 CFR 121.3)

African horse sickness virus
African swine fever virus
Akabane virus
Avian influenza virus (highly pathogenic)
Bluetongue virus (exotic)
Bovine spongiform encephalopathy agent
Camel pox virus
Classical swine fever virus
Ehrlichia ruminantium (Heartwater)
Foot-and-mouth disease virus
Goat pox virus
Japanese encephalitis virus
Lumpy skin disease virus
Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1)
Menangle virus
Mycoplasma capricolum subspecies *capripneumoniae*
(contagious caprine pleuropneumonia)
Mycoplasma mycoides subspecies *mycoides* small colony (*Mmm*SC)
(contagious bovine pleuropneumonia)
Newcastle disease virus (VVND)
Peste des petits ruminants virus
Rinderpest virus
Sheep pox virus
Swine vesicular disease virus
Vesicular stomatitis virus (exotic): Indiana subtypes VSV-IN2, VSV-IN3

Virulent Newcastle disease virus[159]

USDA/APHIS Plant Protection and Quarantine (PPQ) Select Agents and Toxins
(7 CFR 33 1.3)

Peronosclerospora philippinensis (*Peronosclerospora sacchari*)
Phoma glycinicola (formerly *Pyrenochaeta glycines*)
Ralstonia solanacearum race 3, biovar 2
Rathayibacter toxicus
Sclerophthora rayssiae var. zeae
Synchytrium endobioticum
Xanthomonas oryzae
Xylella fastidiosa (citrus variegated chlorosis strain)

[159] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (*Gallus gallus*) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

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ABBREVIATIONS AND ACRONYMS

AAALAC	Association for the Assessment and Accreditation of Laboratory Animal Care International
ABSA	American Biological Safety Association
ABSL	Animal biosafety level
ABSP	Agricultural Biotechnology Support Project II
ACL	Arthropod Containment Levels
AHPA	*Animal Health Protection Act*
AHRQ	Agency for Healthcare Research and Quality
ANSI	American National Standards Institute
APHIS	Animal and Plant Health Inspection Service (USDA)
ARS	Agricultural Research Service (USDA)
ASM	American Society of Microbiology
BAI	Bureau of Animal Industry
BAR	Biological Agent Registration (State of Maryland)
BARDA	Biomedical Advanced Research and Development Authority (HHS)
BBC	Boston Biosafety Committee
BBEP	Biotechnology, Biologics, and Environmental Protection (USDA)
BIS	Bureau of Industry and Security (DOC)
BLS	Bureau of Labor Statistics
BMBL	*Biosafety in Microbiological and Biomedical Laboratories*
BRAC	Boston rDNA Advisory Committee
BRS	Biotechnology Regulatory Services
BSL	Biosafety level
BSO	Biosafety officer
BSC	Biological safety cabinet
CBP	U.S. Customs and Border Protection
CCL	Commerce Control List
CDC	Centers for Disease Control and Prevention
CEN	European Committee for Standardization (Comité Européen de Normalisation)
CFR	Code of Federal Regulations
CGMP	*Current Good Manufacturing Practice* (FDA)
CLIA	Clinical Laboratory Improvement Amendments
CLSI	Clinical and Laboratory Standards Institute
CSIRO	Commonwealth Scientific and Industrial Research Organization (Australia)
CSREES	Cooperative State Research, Education, and Extension Service

DGMQ	Division of Global Migration and Quarantine (CDC)
DHS	Department of Homeland Security
DNA	Deoxyribonucleic acid
DOC	Department of Commerce
DOD	Department of Defense
DOE	Department of Energy
DOL	Department of Labor
DOT	Department of Transportation
DSAT	Division of Select Agents and Toxins (CDC)
EAIPP	Etiologic Agent Import Permit Program (CDC)
ECP	Exposure Control Plan
EPA	Environmental Protection Agency
FAA	Federal Aviation Administration
FAD	Foreign animal disease
FDA	Food and Drug Administration
FERN	Food Emergency Response Network
FIFRA	*Federal Insecticide, Fungicide, and Rodenticide Act*
FSIS	Food Safety and Inspection Service (USDA)
GLP	*Good Laboratory Practice* (Regulations) (FDA)
GAO	Government Accountability Office
HHS	(Department of) Health and Human Services
HIV	Human Immunodeficiency Virus
HMR	*Hazardous Materials Regulations*
IACUC	Institutional Animal Care and Use Committee
IATA	International Air Transport Association
IBC	Institutional Biosafety Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
LAI	Laboratory-acquired infection
LRN	Laboratory Response Network
MDR-TB	Multidrug-resistant tuberculosis
NAHLN	National Animal Health Laboratory Network
NAICS	North American Industry Classification System
NASA	National Aeronautics and Space Administration
NBAF	National Bio- and Agro-Defense Facility
NBBTP	National Biosafety and Biocontainment Training Program
NBL	National Biocontainment Laboratories
NEP	National Emphasis Program (OSHA)

NHSN	National Healthcare Safety Network (CDC)
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NIH Guidelines	*NIH Guidelines for Research Involving Recombinant DNA Molecules*
NIOSH	National Institute for Occupational Safety and Health
NSABB	National Science Advisory Board for Biosecurity
NSF	National Sanitation Foundation
OBA	Office of Biotechnology Activities (NIH)
OHRP	Office for Human Research Protections
OSHA	Occupational Safety and Health Administration
PBS	Program for Biosafety Systems
PHMSA	Pipeline and Hazardous Materials Administration (DOT)
PHS	Public Health Service (HHS)
PI	Principal Investigator
PPA	*Plant Protection Act*
PPE	Personal Protective Equipment
PPQ	Plant Protection and Quarantine
PSO/NPSD	Patient Safety Organization-Network of Patient Safety Databases
R&D	Research and Development
RBL	Regional Biocontainment Laboratories
rDNA	Recombinant DNA
RNA	Ribonucleic acid
RO	Responsible Official
SARS	Severe acute respiratory syndrome
SIC	Standard Industrial Classification
TB	Tuberculosis
U.S.	United States
USAID	U.S. Agency for International Development
U.S.C.	United States Code
U.S.C.A.	United States Code Annotated
USDA	United States Department of Agriculture
VSTA	*Virus-Serum-Toxin Act*
WHO	World Health Organization
WMD	Weapons of mass destruction
XDR-TB	Extensively drug-resistant tuberculosis

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APPENDICES

APPENDIX A

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APPENDIX B

Charge of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight

Notes:

1. *All Federal agencies and departments with a role in the conduct or oversight of research with hazardous biological materials should participate in efforts to improve biosafety and biocontainment oversight.*
2. *The report of the Task Force should serve as the impetus for developing mechanisms to provide a seamless net of biosafety and biocontainment oversight encompassing research in high and maximum containment laboratories in the public, academic, and private sectors, as well as in the Federal sector.*

New scientific tools and understanding have created unprecedented opportunities for progress in life sciences research, including discoveries of the molecular mechanisms by which certain microbes cause disease, and the means by which new infectious disease threats can emerge. These opportunities can enable many important advances in medicine, public health, and agriculture. Coincident with this era of opportunity have been elevated concerns about bioterrorism as well as criminal acts involving the use of biological agents, giving rise to an urgent need for the rapid development of diagnostics, vaccines, and other biodefense-related medical countermeasures. Research into these areas has become a national priority, with increased Federal support for programs to promote scientific investigation in academic and commercial settings, as well as in Federal research facilities.

The importance of effective biosafety and biocontainment practices and oversight of activities involving work with potential biological hazards (infectious disease-causing organisms and biological toxins) at individual research institutions and Federal agencies cannot be overemphasized. Although the Federal Government is committed to ensuring the highest quality design and construction of high and maximum containment facilities, the rigorous training of personnel who work in them, and the safe conduct of research undertaken in them, there are areas of concern. Press reports, articles in scientific publications,[160] Government Accountability Office reports,[161,162] and a report by the

[160] Kaiser J. Biosafety breaches: Accidents spur a closer look at risks at biodefense labs. *Science*. 2007. 317 (5846):1852-1854.
[161] U.S. Government Accountability Office. *HIGH-CONTAINMENT BIOSAFETY LABORATORIES, Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*. 2007. GA0-08-108T.
[162] U.S. Government Accountability Office. *Biosafety Laboratories: Perimeter Security Assessment of the Nation's Five BSL-4 Laboratories*. 2008. GAO-08-1092. HHS/CDC has provided corrections to the GAO preliminary report but a revised, corrected version has not been published as of June 2009.

Commission on the Prevention of WMD Proliferation and Terrorism,[163] as well as congressional concerns have focused attention on the issues of biosafety and biosecurity[164] at high and maximum containment laboratories.

On October 4, 2007, the House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations, held a hearing entitled "Germs, Viruses, and Secrets: The Silent Proliferation of Bio-Laboratories in the United States." At the hearing, subcommittee members voiced concerns about what they viewed as the risks associated with the proliferation of high and maximum containment laboratories (biosafety level 3 [BSL-3] and biosafety level 4 [BSL-4] and their agricultural equivalents) in the United States. At issue was the status of Federal oversight of BSL-3, BSL-4, and equivalent containment facilities, including the number and locations of all BSL-3 facilities.

At the October 2007 hearing, agency representatives from the U.S. Department of Health and Human Services (HHS) announced the establishment of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (Task Force). The Task Force was established to undertake an intensive analysis of the current framework of biosafety and biocontainment oversight of high and maximum containment research on hazardous biological agents and toxins, with the goal of exploring strategies to address concerns voiced by Congress and the general public.

The Task Force is chaired by officials from HHS and the U.S. Department of Agriculture (USDA), and is comprised of representatives from a broad range of Federal departments and agencies that have responsibility for, and oversight of the management of biohazard risks. Included in the Task Force are members from HHS, USDA, and the Departments of Commerce, Defense, Energy, Homeland Security, Labor, State, Transportation, and Veterans' Affairs, as well as the Environmental Protection Agency and the National Science Foundation (see Appendix A).

Task Force Charge and Vision

The purpose of the Task Force is to propose options and recommendations to improve biosafety and biocontainment oversight of research activities at high and maximum containment research laboratories in the United States through a comprehensive review of mechanisms by which individual research (local) institutions and the Federal Government can ensure safe working conditions (see Appendix B). The Task Force envisions effective, comprehensive, local (institutional) and Federal oversight that

[163] *World at Risk: The Report of the Commission on the Prevention of WMD Proliferation and Terrorism*. Released December 2, 2008. See http://www.preventwmd.gov/report/.

[164] In addition, Executive Order 13486, entitled *Strengthening Laboratory Biosecurity in the United States*, signed on January 9, 2009, by former President George W. Bush, ordered the establishment of the Working Group on Strengthening the Biosecurity of the United States. The new working group is charged with preparing a report on laboratory biosecurity and personnel reliability, topics that are related to biosafety. Executive Order 13486 is available at http://fas.org/irp/offdocs/eo/eo-13486.htm.

protects laboratory workers, public health, agriculture, and the environment, without hindering the progress of science. The Task Force was charged to present this report to the USDA and HHS Secretaries for their consideration.

Scope of Activity

The scope of research activities considered by the Task Force includes those that occur in all high and maximum containment laboratory research facilities in all sectors (Federal, State, academic, private, and commercial laboratories) utilizing potentially hazardous biological agents (pathogens and toxins).

Beyond the scope of the Task Force report are activities involving select agents that take place in diagnostic and treatment (non-research) facilities such as hospitals, clinics, veterinary, and food diagnostic laboratories. These include some laboratories associated with the National Animal Health Laboratory Network (NAHLN) and the Food Emergency Response Network (FERN). Most licensed biomedical production facilities and mobile field analytical laboratories also lie outside the scope of this report because they are not research facilities. The activities of these facilities vary markedly from those engaged in high and maximum containment research.

Although this report offers a brief discussion of the relationship between laboratory biosecurity and biosafety, laboratory biosecurity *per se* is not the focus of this report. The term "laboratory biosecurity" denotes the protection of hazardous biological agents, including toxins, from loss, theft, diversion, or intentional misuse. Good biosafety and biocontainment practices contribute to effective laboratory biosecurity, and the disciplines of biosafety and laboratory biosecurity are complementary in many aspects. However, the Task Force did not want to deviate substantially from its focus on biosafety and biocontainment oversight.

Approach

In developing the report, the working group of the Task Force focused on:

- Conducting a comprehensive assessment of the current biosafety/biocontainment oversight framework for high and maximum containment laboratory research activities and facilities in all sectors. Oversight is achieved at many levels, the most critical of which are individual research institutions ("local oversight") and Federal entities such as HHS/CDC and USDA/APHIS ("Federal oversight"). The Task Force review encompassed the identification and assessment of pertinent laws, regulations, policies, standards, and guidelines in addition to examining current biosafety/biocontainment oversight mechanisms in use by local institutions as well as municipal, State, and Federal oversight entities.

- Developing specific objectives for improving the current biosafety/biocontainment oversight framework. The objectives are based on identifying issues and needs related to the current biosafety/biocontainment oversight framework for high and maximum containment laboratories in which research on hazardous biological agents is conducted.

- Developing options and recommendations for achieving the objectives. In efforts to explore strategies that best meet the biosafety and biocontainment needs of Federal and non-Federal research involving biological hazards, Task Force members endeavored to strike a balance among solutions to optimize biosafety and biocontainment oversight and the potential impact of increased oversight. **The focus was on devising a framework that improves biosafety and biocontainment oversight, incident-reporting, and training without causing unintended negative consequences for progress in research.**

The working group's process of deliberation and consultation also included soliciting the perspectives and input from key stakeholders. A public consultation meeting was held December 8−9, 2008. Based on input from those who attended the meeting or submitted comments to the website established for that purpose, the Task Force further developed and revised this report.

Engaging the public as a key stakeholder is vital given the critical importance of biosafety and biocontainment oversight for protecting laboratory workers, public health, agriculture, and the environment. Public engagement also is critical to address the concerns of communities in which high and maximum containment facilities are located or planned, because of public perception that these facilities could adversely affect public health or the environment. The Task Force recognizes that extensive consultation with the researchers, biosafety professionals, and science administrators responsible for high and maximum containment research facilities also is crucial for implementing measures to enhance the existing framework for biosafety and biocontainment oversight, and for ensuring the measures are appropriate, practical, and acceptable.

Continued strengthening of biosafety/biocontainment oversight of research at high and maximum containment facilities in all sectors will require informed action on the part of the Federal Government; State and municipal authorities; experts in biosafety and biocontainment; scientists; professional organizations; and the public. It is the expectation of the Task Force that its recommendations will lead to the development and implementation of an optimized framework for biosafety and biocontainment oversight.

APPENDIX C

Scope of Federal Biosafety and Biocontainment Oversight

Scope	Activity	Federal Agency/Department (nature of policy)	Citation	Entity Covered
Serious workplace hazards (including biological agents and toxins)	All activities in the workplace	U.S. Department of Labor/OSHA (statute)	▪ 29 U.S.C. 654 Section 5(a)(1) (*General Duty Clause*)	All employers covered by the *OSH Act* (regardless of Federal funding)
Bloodborne pathogens	All work that involves occupational exposure to bloodborne pathogens or potentially infectious materials	U.S. Department of Labor/OSHA (regulation)	▪ 29 CFR 1910.1030 (*Bloodborne Pathogens Standard*)	All employers covered by the *OSH Act* (regardless of Federal funding)
Hazards necessitating the use of personal protective equipment (PPE) (including biological agents and toxins)	All work that where hazards are present that necessitate the use of PPE	U.S. Department of Labor/OSHA (regulation)	▪ 29 CFR 1910 subpart I (*Personal Protective Equipment Standards*)	All employers covered by the *OSH Act* (regardless of Federal funding)
All covered hazards (including biological agents and toxins)	All workplaces where a covered hazard is present	U.S. Department of Labor/OSHA (regulations)	Other applicable OSHA standards: ▪ 29 CFR 1910.120 (*Hazardous Waste Operations and Emergency Response*) ▪ 29 CFR 1910.141	All employers covered by the *OSH Act* (regardless of Federal funding)

Scope	Activity	Federal Agency/Department (nature of policy)	Citation	Entity Covered
			(*Sanitation*) ▪ 29 CFR 1910.151 (*Medical Services and First Aid*) ▪ 29 CFR 1910.1020 (*Access to RR Exposure and Medical Records*) ▪ 29 CFR 1910.1200 (*Hazard Communication*) ▪ 29 CFR 1910.1201 (*Retention of DOT Markings, Placards and Labels*) 29 CFR 1910.1450 ▪ (*Occupational Exposure to Hazard Chemicals in Laboratories)*	
Biological agents	All workplaces where a specific biological agent is present	U.S. Department of Labor/OSHA (guidelines/guidance information)	Safety and Health Information Bulletin (SHIB) For example: ▪ Workplace Precautions Against West Nile Virus Safety and Health Topics Pages – Biological Agents For example: ▪ Anthrax ▪ Plague	All employers covered by the *OSH Act* (regardless of Federal funding)

Scope	Activity	Federal Agency/Department (nature of policy)	Citation	Entity Covered
			▪ Ricin ▪ Smallpox ▪ Tularemia ▪ Worker Safety and Health Guidance for H1N1 Flu eTools For example: ▪ Hospital eTool: *Laboratory Module*	
Infectious agents	Interstate transfer of infectious agents	U.S. Department of Transportation (regulation)	▪ 49 CFR 173 (*Transportation of Etiologic Agents*)	All shippers (regardless of Federal funding)
	Exportation of etiologic agents	U.S. Department of Commerce (regulation)	▪ 15 CFR 730-774 (*Export Administration Regulations*)	All exporters (regardless of Federal funding)
	Importation and interstate movement of infectious agents and agricultural pathogens and pests	U.S. Department of Health and Human Services/CDC; U.S. Department of Agriculture/APHIS (regulations)	▪ 42 CFR 71.54 (*Etiologic agents, hosts, and vectors*) ▪ 7 CFR 330 (*Federal Plant Pest Pathogens Regulations*) ▪ 9 CFR 92 (*Importation of Animals and Animal Products*) ▪ 7 U.S.C. 7701 *et seq*. (*Plant Protection Act*) ▪ 7 U.S.C. 8301 *et seq*. (*Animal Health Protection Act*)	All importers or institutions involved in interstate movement of regulated materials (regardless of Federal funding)

Scope	Activity	Federal Agency/Department (nature of policy)	Citation	Entity Covered
			▪ 9 CFR 101-118 (Veterinary biologics) ▪ 9 CFR 122 (Organisms and vectors) ▪ 7 CFR 340 (Genetically modified organisms that are plant pests)	
	Handling of infectious agents in laboratory settings	U.S. Department of Health and Human Services/CDC and NIH (guidelines)	▪ *Biosafety in Microbiological and Biomedical Laboratories* (Includes guidelines on occupational medicine and immunization, decontamination and sterilization, and laboratory biosecurity and risk assessment. Agent summary statements and appendices are updated periodically)	Voluntary for most entities; mandatory for intramural research at NIH
Select Agents and Toxins	Possession, use, and transfer	U.S. Department of Health and Human Services/CDC; U.S. Department of Agriculture/APHIS (regulation)	▪ 42 CFR 73 (*Select Agent Regulations* - CDC) ▪ 9 CFR 121 and 7 CFR 331 (*Select Agent Regulations* - APHIS)	All entities that possess, use, or transfer select agents
Recombinant DNA-modified infectious agents	Research utilizing recombinant DNA-modified	U.S. Department of Health and Human Services/NIH (guidelines)	▪ *NIH Guidelines for Research Involving Recombinant DNA Molecules*	Recipients of NIH funding for recombinant DNA research

Scope	Activity	Federal Agency/Department (nature of policy)	Citation	Entity Covered
	infectious agents			
Food, drugs, and cosmetics	Safety and purity standards for foods, drugs, and cosmetics manufactured in the U.S.	U.S. Department of Health and Human Services/FDA (regulations)	▪ 21 CFR 56 (*Good Laboratory Practice for Nonclinical Laboratory Studies*) ▪ 21 CFR 26, Subpart A (*Specific Sector Provisions for Pharmaceutical Good Manufacturing Practices*)	Manufacturers of products regulated by FDA

APPENDIX D

DOL (BLS) Sample Survey Results – 2006: Scientific Research and Development Injury and Illness Data*

The table below provides a summary of the Department of Labor (DOL) Bureau of Labor Statistics (BLS) sample survey of injury and illness data of the labor force at scientific research and development (R&D) facilities (Category NAICS 5417)[165] for calendar year 2006. The survey includes injury and illness statistics from a wide range of private scientific R&D facilities, i.e., information technology; environmental and ecological services; chemical, electrical, and mechanical engineering; biological, physical science, and social science facilities; and entities that employ medical scientists. Some data from high and maximum containment facilities might be included in the 2006 survey, although it is not possible to determine their inclusion from the survey results. Not all private R&D facilities were surveyed, and no Federal high or maximum containment research facilities were surveyed.

Based on the injury and illness data from the 2006 sample survey, the overall injury and illness rates for scientific R&D facilities are well below the national average for general private industry:

- Number of injury and illness cases reported in general industry overall was 4,085,400 versus 8,100 reported cases in scientific R&D facilities (NAICS 5417). Based on these cases, the overall rate of injury and illnesses among workers in general industry was 4.4 versus 1.4 in scientific R&D facilities.
- Number of cases involving days away from work, job transfer, or restriction (DART, meaning days away, restricted, or transferred) was 2,114,600 in general industry versus 3,500 in scientific research facilities. Based on this information, the corresponding DART rates were 2.3 for general industry overall and 0.6 for scientific R&D facilities.

Number and Rate of Occupational Injuries and Illnesses for All Private Industry and Private Scientific R&D Facilities, 2006

Characteristics	All Private Industry		Scientific Research and Development Facilities*	
	Number (in thousands)	Rate	Number (in thousands)	Rate
Injuries and Illnesses				
Total cases	4085.40	4.4	8.1	1.4
Cases w/days away from work, job transfer, or restriction	2114.60	2.3	3.5	0.6
Cases w/ days away from work (2)	1183.50	1.3	2	0.4

[165] For a definition of NAICS code 5417, see http://www.census.gov/cgi-bin/sssd/naics/naicsrch. The BLS web site at http://www.bls.gov/oco/cg/cgs053.htm also contains information about this industry.

Cases w/ job transfer or restriction	931.1	1	1.5	0.3
Other recordable cases	1970.8	2.1	4.6	0.8
Injuries				
Total cases	3857.4	4.2	6.9	1.2
Illnesses				
Total cases	228	24.6	1.3	22.3
Illness categories				
Skin disorders	41.4	4.5	0.1	2.1
Respiratory conditions	17.7	1.9	0.1	1.3
Poisoning	3.4	0.4	* (< 15 cases)	-
Hearing loss	24.4	2.6	** (<50 cases)	0.7
All other illness cases	141.1	15.2	1	18.2

Key for Table:
(1) Injury rates represent the number of injuries and illnesses per 100 full-time workers (10,000 full-time workers for illness rates) and were calculated as: (N/EH) X 200,000 (20,000,000 for illness rates where,
N = number of injuries and illnesses,
EH = total hours worked by all employees during the calendar year,
200,000 = base for 100 full-time equivalent workers (working 40 hrs per week, 50 weeks per year).
20,000,000 = base for 10,000 full-time equivalent workers (working 40 hrs per week, 50 weeks per year).
(2) Days away from work cases include those that result in days away from work with or without job transfer or restriction

NOTE: Dashes represent data that do not meet BLS publication guidelines

*****High and maximum containment research facilities that house biologic hazards fall under the general category of scientific research and development services. Data are not available for high and maximum containment research facilities alone.

APPENDIX E

Suggested Roles and Responsibilities for Biosafety Professionals and Local Biosafety Review Committees

High and maximum containment research facilities have in place various biosafety professionals and mechanisms to provide biosafety and biocontainment oversight of their laboratories. The 5th edition of the *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*, Section III, "Principles of Biosafety") specifies the need for biosafety professionals and an institutional body dedicated to managing biohazard risk. The roles and responsibilities of biosafety professionals and local biosafety review committees (institutional biosafety committees[IBCs] and equivalents) that help assess the risks of research involving infectious agents and other potential biohazards varies from one institution to another, depending on the nature of research and the facility.

The duties of BSOs are formally defined under the *NIH Guidelines*[166] for the oversight of research with rDNA agents; their presence is mandated for institutions conducting large-scale rDNA research or rDNA work in high (BSL-3) or maximum (BSL-4) containment laboratories. The following suggested roles and responsibilities of biosafety professionals and local biosafety review committees expand on the information described in Chapter III, and are designed to enhance local biosafety/biocontainment oversight of research at individual high and maximum containment research facilities.

Biosafety Professionals

The requirements and specific responsibilities of institutional biosafety professionals (biosafety officers [BSOs] and equivalent professionals) at all high and maximum containment research facilities in all sectors would need to be formulated, but could include the following activities, done in collaboration with local biosafety review committees and investigators:

- Assess the risk of occupational exposure and infection associated with handling hazardous biological agents and toxins, and—in collaboration with local biosafety review committees—communicate to laboratory workers the level of risk and means to reduce exposures to or releases of infectious organisms (although individual institutions could develop different, yet still effective, mechanisms for risk assessment)

- Help manage biohazard risk, e.g., by participating in the assignment of the appropriate level of containment for work with these agents

[166] Duties of BSOs are described in the *NIH Guidelines*, Section IV-B-3-c, and are available at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html.

- Conduct periodic inspections and audits to ensure that laboratory biosafety/biocontainment practices and procedures are rigorously followed

- Ensure the infrastructure of high and maximum containment facilities is appropriately maintained, and that facility operations, in addition to actual laboratory operations, at these facilities in all sectors are safe

- Participate in facility design, operation and renovation planning processes. The biosafety professional should conduct or oversee design review of proposed facility designs/modifications, acceptance testing procedures, and system modification activities.

- Act as a liaison to a senior institutional official who provides assurances to a Federal biosafety/biocontainment coordinating entity (should such an entity be established) or other oversight entity on a broad range of biosafety and biocontainment issues including the technical competence and training status of essential personnel, standards for and status of facility accreditation (if the facility is accredited), laboratory incidents, construction or expansion of high and maximum containment laboratories, etc.

- Inform relevant authorities about the activities of the laboratory through routine reports, authorization requests, descriptions of safety measures employed, inspections, etc.

- Report to the local biosafety review committee and appropriate institutional official(s) any significant problems, violations of relevant regulations, and any significant research-related accidents, incidents, or illnesses

- Interpret and enforce regulations and guidelines relevant to the safety, containment, and security of working with hazardous biological agents and toxins

- Provide technical advice about biosafety/biocontainment practices and procedures to principal investigators (PIs) and the local biosafety review committee

- Help provide institution-specific training on policies and procedures that are needed to work safely in the institution's laboratories

- Assist in the development of emergency plans for handling accidental spills and personnel contamination, and investigating laboratory accidents and other incidents

- Have appropriate authority to perform and implement institutional biosafety policies

Local Biosafety Review Committees

Under the *NIH Guidelines*, Institutional Biosafety Committees (IBCs) are mandated only to review recombinant DNA research at institutions that receive NIH funding for this type of research. To the extent that these and equivalent committees would assume additional research review responsibilities for all research taking place in high and maximum containment facilities at institutions regardless of funding source, that mandate needs to be formally and specifically defined and should address the roles and responsibilities, review procedures, and functions of local biosafety review committees in that new context. Their mandate might include the following, carried out in collaboration with institutional biosafety professionals and PIs:

- Establish and improve, when necessary, formalized mechanisms for assessing the risks of working with the particular hazardous biological agents and toxins under study at the institution, and conduct risk assessments before studies of these agents begin (although individual institutions could develop different, yet still effective, mechanisms for risk assessment)

- Review all research protocols—in collaboration with the biosafety professional(s)—to determine and recommend to the PI(s) or laboratory supervisor the appropriate level of containment needed to work safely with each of the biohazards under study

- Help ensure that all laboratory personnel[167] and biosafety professionals have the requisite biosafety/biocontainment training and experience, and assess their biosafety/biocontainment expertise

- Help ensure individual and institutional compliance with biosafety and biocontainment Federal, State, and municipal regulations and guidelines (the *BMBL* and other relevant guidelines), and have the authority to enforce compliance with decisions, applicable policies, and requirements

- Review laboratory incidents, including accidents, significant exposures to biological hazards, and possible laboratory-acquired infections (LAIs), and conduct incident investigations as appropriate

[167] As used in this report, the term "all laboratory personnel" encompasses the following: (1) PIs, laboratory supervisors, researchers, and technicians (including those with and without formal training in laboratory safety, and any students who work in BSL-3 facilities), (2) animal care and support staffs (including security and housekeeping staff); (3) facilities and engineering staff (including those who maintain the associated systems of these facilities such as the specialized air-flow systems that are specific to high and maximum containment laboratories); (4) institutional biosafety professionals (biosafety officers [BSOs] and their equivalents) and members of biosafety review committees (institutional biosafety committees [IBCs] and their equivalents); (5) individuals, including senior institutional officials, who have overall management responsibilities for these facilities; and (6) individuals who review and inspect the facilities.

- Review and adopt emergency plans for handling accidental spills or releases outside of primary containment (biosafety cabinets, personal protective equipment, etc.)

- Report, as appropriate, problems with or violations of regulations, and any significant research-related accidents or illnesses to the appropriate institutional official(s) and relevant Federal, State, or municipal entities (i.e., in the event of a containment breach, accidents involving human exposure, administrative errors, etc.)

- Review and update institutional biosafety management program-related materials (including policies, plans, manuals, and procedures)

- Establish a system for informing laboratory personnel about new risks in the laboratory (changes in the agents under study, changes in experimental protocols with existing agents, etc.)

- Review and strengthen, if necessary, occupational health programs and develop mechanisms to ensure that attending physicians are informed about the risks of working with hazardous biological agents and the symptoms an infected laboratory worker under their care may exhibit

APPENDIX F

Examples of Federal Outreach and Education Activities

Federal outreach and education activities that pertain to biosafety and biocontainment at high and maximum containment research facilities target two key audiences: Federal and non-Federal entities that conduct research. These efforts are not specific to the BSL-3, BSL-4, and equivalent containment research facilities that are the focus of this report, but are more general.

Federal departments and agencies with responsibility for the conduct and oversight or research and research-related activities at high and maximum containment facilities take steps to ensure that constituency groups and collaborators in all sectors (government [Federal, State, Tribal, and municipal], academia, privately funded research institutions, and private industry) are aware of biosafety regulations, and guidelines; are informed about changes to regulations and guidelines; and understand the importance of complying with them. Education and outreach activities targeted to entities that conduct research vary across Federal entities, and can include posting relevant biosafety/biocontainment information online, encouraging participation at conferences and meetings, distributing educational materials, and conducting outreach to stakeholders in the research community.

Department of Health and Human Services (HHS) – National Institutes of Health (NIH)

NIH, a component of HHS, has long been a leader in biosafety awareness and training. In 1964, Congress provided funds to NIH for intensive research into the possible role of viruses in leukemia. In 1968, the program then titled the Special Virus Cancer Program, was enlarged to encompass all types of cancer. On July 1, 1973 the Special Virus Cancer Program was renamed The Virus-Cancer Program (VCP) "to integrate the Program's research activities into the framework of the new National Cancer Plan."

Early biosafety awareness and guidance documents were produced by the National Cancer Institute (NCI) during the Special Cancer Virus Program. These documents included "*The National Cancer Safety Standards for Research Involving Oncogenic Viruses*" and a variety of Cancer Research Safety Monographs resulting from the Cancer Research Symposia. These publications and the Laboratory Safety Monograph (prepared by the Office of Research Safety, National Cancer Institute as a supplement to the *NIH Guidelines* in 1979) are still used today.

In the mid-1970s, when recombinant DNA (rDNA) was an emerging technology, the NIH developed—with broad participation of the scientific community and the public—national biosafety and containment standards for rDNA research in the form of the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*).

NIH's current activities designed to raise awareness and understanding of the *NIH Guidelines* are described below.

In 1984, CDC and NIH published the first edition of the laboratory guidance document, *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*). The *BMBL* is used widely and has been revised to keep pace with the needs of science and society; it is now in its fifth edition.

In the context of NIH-funded research programs involving rDNA, the NIH Office of Biotechnology Activities (OBA) has made it a priority to develop mechanisms for outreach and education that are multifaceted and address various audiences with key responsibilities for upholding the biosafety principles and practices of the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (*NIH Guidelines*). The primary audience for these programs includes members of institutional biosafety committees (IBCs). Other important audiences for OBA outreach program include laboratory investigators, research administrators (notably managers of Institutional Review Boards [IRBs] and Institutional Animal Care and Use Committees [IACUCs]), and officials at institutions subject to the *NIH Guidelines* who have overarching administrative and management responsibilities for research programs. The OBA outreach program involves electronic media, printed materials, and presentations.[168]

In November 2006, OBA launched a site visit program to help enhance compliance with the *NIH Guidelines* and gain information about institutions subject to the *NIH Guidelines*.[169] The site visit program is an essential element of OBA outreach activities because it offers a tailored and interactive experience, providing a forum for the institutional representatives to ask questions, make informed enhancements to the IBC program, and incorporate best practices. To date, OBA has visited a diverse set of institutions (universities, medical schools, research institutes, and companies) that conduct varied types of research programs (with emphasis on clinical, basic biomedical, and agricultural programs).

In addition to helping institutions improve their IBC programs in the immediate term, the site visit program aims to assist in the longer term by:

- Identifying common compliance challenges facing institutions for the purpose of tailoring our educational programs to assist institutions in overcoming them
- Developing a body of best practices that institutions may consider, as appropriate to optimize the functioning of their own programs
  Creating a self-evaluation tool that allows institutions to assess and improve their own IBC programs.

[168] The OBA web site provides basic information to those who need to understand the roles and responsibilities of IBCs. For more information, see http://oba.od.nih.gov/rdna_ibc/ibc.html.
[169] Information about the NIH OBA site visit program is available at http://oba.od.nih.gov/oba/ibc/FAQs/FAQs%20about%20the%20NIH%20OBA%20Site%20Visit%20Program.pdf.

Department of Health and Human Services – Centers for Disease Control and Prevention (CDC)

CDC provides strong leadership on a range of topics from biosafety to public health, clinical, and research communities through the development and distribution of documents and other materials, coordinating and delivering training programs, sponsoring conferences and symposia, and providing advice.

Specific outreach and education activities in the area of biosafety are identified below. Some have been developed and promoted by CDC; others were done in collaboration with strategic partners. The most significant partners include the NIH OBA, the U.S. Department of Agriculture (USDA), and the National Laboratory Training Network (NLTN), which is a collaboration with the Association of Public Health Laboratories (APHL) and the CDC.

- CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition)*
- CDC/Division of Select Agents and Toxins Video:[170] "Biosafety Level-3 Inspection Process" (per *BMBL*)
- CDC/NIH Biosafety Cabinet Pamphlet (*Primary Containment for Biohazards: Selection, Installation, and Use of Biological Safety Cabinets*)
- Select agent guidance documents and training videos[171]
- CDC slide set: "Biosafety in the Laboratory"[172]
- CDC Biosafety Conference: Advanced Topics in Managing BSL-3 Laboratories, Atlanta GA – January 2009
- CDC International Biosafety Symposium (held every 2 years). Recent conferences include "Protecting Workers in Clinical Laboratories, Research, Animal Care, and Public Health Communities", Atlanta, GA – February 2008; "Occupational Health Care and Medical Surveillance for Laboratory Animal Care Workers", Atlanta GA – February 2006
- CDC/USDA Biosafety Training Modules - *Principles of Biosafety in BSL-2 Laboratories* (1 week of classroom modules; product midway in development)
- CDC/NLTN training courses[173] (variety of courses including those below):
    - *Biosafety: Assessing the Risk*
    - *Packaging and Shipping Division 6.2 Materials*
    - *Biosafety and Biosecurity: Minimizing Risks in the Laboratory*

[170] Informational videos prepared by CDC and APHIS on BSL-3 facility inspection under the *Select Agent Regulations* are available at http://www.selectagents.gov/FacilityInspectionDVD.htm.
[171] The select agent guidance documents and training videos are available on the national select agent website at www.selectagents.gov.
[172] The CDC slide set "Biosafety in the Laboratory" is available at http://www.cdc.gov/od/ohs/biosfty/biosfty.htm.
[173] CDC/NLTN training courses are available at http://www.aphl.org/profdev/training/Pages/default.aspx.

- CDC Training Video: "Laboratory Risk Assessment – What, Why, and How" (1998)

U.S. Department of Agriculture (USDA)

USDA has supported outreach efforts focused on biosafety awareness and training.

- USDA/APHIS – Fact Sheet: *Biosecurity: Protecting Your Livestock and Poultry March 2007*[174]
- USDA/FSIS – Provides biosafety training for FERN laboratories

USDA and HHS

Some efforts focused on biosafety and biocontainment are sponsored jointly by the USDA/Agricultural Research Service (ARS) and HHS/CDC.

- Collaboration and Stakeholders meeting (2009). Efforts also are being undertaken to strengthen global partnerships between Ministries of Health and Agriculture, because both entities must have adequate laboratory capacity to recognize and respond to incidents that could threaten public health or agriculture. The primary purpose of the stakeholders meeting is to ensure that a mechanism is created to provide biosafety support and assistance to the Ministries of Health and Agriculture that are beginning to conduct work with high-consequence pathogens.
- CDC and ARS standardized training program (nine modules) on the *Principles of Biosafety in BSL-2 Laboratories* (in development)
- CDC and APHIS Select Agent Workshops

Department of Homeland Security (DHS)

The Department of Homeland Security (DHS) Regulatory Compliance Office (RCO), which is operated within the Science and Technology Directorate, is responsible for implementing and ensuring Department-wide compliance with DHS policies for biosafety and select agent and toxin security. To support this mission, the RCO conducts extensive outreach to DHS components and sponsored institutions performing biological laboratory activities for the Department. These outreach efforts, which focus specifically on enhancing awareness of and compliance with biosafety-related requirements, standards, and practices, include:

- Delivering briefings and providing informational materials to DHS components and program managers on Federal and Departmental requirements and guidelines governing biological laboratory work

[174] The USDA fact sheet is available at http://www.aphis.usda.gov/publications/animal_health/content/printable_version/fs_bio_sec_07.pdf.

- Conducting site visits to institutions performing DHS-sponsored biological research projects to review and provide guidance on biosafety-related programs, training, practices, and oversight mechanisms
- Engaging principal investigators and other research personnel conducting biological laboratory work for DHS to: facilitate awareness and understanding of biosafety requirements, standards, and guidelines; identify and address biosafety questions and concerns; and share best practices for enhancing biosafety and biosecurity

The RCO also is collaborating with other Federal agencies, policy development committees, and stakeholder groups to harmonize DHS outreach efforts with those of Federal oversight authorities, and to support the advancement of standardized requirements and guidance for biosafety.

Department of Labor (DOL) – Occupational Safety and Health Administration (OSHA)

Through an Alliance with the American Biological Safety Association (ABSA), the Department of Labor (DOL), Occupational Safety and Health Administration (OSHA), has conducted annual outreach and training for biosafety professionals. The OSHA Directorate of Enforcement Programs has provided speakers to present occupational safety and health information in the general session of ABSA's annual meetings.

In 2005, OSHA developed a Professional Development Course (PDC) that has been taught at the ABSA annual conference for 3 consecutive years. The PDC entitled, "Introduction to OSHA for Biosafety Professionals", provide participants with a basic understanding of OSHA and its inspection policies and procedures. The training includes discussion of the application of OSHA's safety and health standards for biocontainment laboratories, including extensive guidance on the OSHA *Bloodborne Pathogens Standard*, *Respiratory Protection Standard*, *Hazard Communication Standard,* and *Laboratory Standard*. In addition, training covers the OSHA *General Duty Clause* [Section 5(a)(1)] and its application to biological hazards in the workplace, as well as current OSHA policy regarding indoor air quality.

The OSHA Directorate of Cooperative and State Programs, the division with the responsibility for forming the OSHA Alliances, has worked closely with ABSA to develop outreach tools, including several fact sheets (on select agents; zoonotic diseases, and the principles of biosafety) which are publicly available on the OSHA-ABSA Alliance webpage.[175]

[175] For information about the OSHA-ABSA Alliance, see http://www.osha.gov/dcsp/alliances/absa/absa.html. To obtain the fact sheets mentioned, see http://www.osha.gov/dcsp/alliances/absa/absa.html#products.

OSHA also has developed and disseminated on its webpage (www.osha.gov) an extensive amount of guidance and technical information for employers and employees about some of the most virulent and prevalent biological agents and toxins. The information includes workplace measures and precautions to prevent or control exposure to hazardous agents, accidents, injuries, and illness. For example, OSHA has established Safety and Health Topics pages for many biological agents including anthrax, botulism, plague, ricin, smallpox, and tularemia (see Appendix C). Most recently, OSHA published information on Workplace Safety and Health Guidance on the novel H1N1 influenza virus on the agency webpage.

APPENDIX G

Accreditation of Biosafety/Biocontainment Management Programs

One potential mechanism for encouraging a culture of increased accountability and compliance with biosafety and biocontainment standards is to establish a system for accrediting biosafety/biocontainment management programs at individual high and maximum containment research institutions (see Objective 2).

For the purposes of this report, the term "accreditation" refers to an objective assessment by an independent body of an institution's biosafety/biocontainment or biorisk management program. Accreditation would allow the institution to demonstrate that its biosafety and biocontainment programs meet or exceed national standards. This approach is comparable to the CEN *Laboratory Biorisk Management Standard*,[176] which indicates "… a biohazard or biorisk management program is that part of an organization's management system used to develop and implement its policy established to manage its biohazards. A management system approach to biohazard risks implies that identifying, understanding and managing a system of interrelated processes for a given objective, improves the organization's effectiveness and efficiency."

Also, according to the CEN standard, "application of the management systems approach principle leads to the following actions:

- Defining the system by identifying or developing the processes that affect a given objective;
- Structuring the system to achieve the objective in the most effective manner;
- Understanding the interdependencies among the processes of the system;
- Continually improving the system through measurement and evaluation, and;
- Establishing resource constraints prior to action."

Thus, according to the CEN standard, "a biorisk management system approach enables an organization to effectively identify, monitor and control the laboratory biosafety, biocontainment and security aspects of its activities…. In order to improve biorisk management an organization needs to focus on the causes of non-conformities and undesirable events (e.g., incidents, accidents, regulatory violations, etc). Systematic identification and correction of system deficiencies leads to improved performance and control of biohazard risk."

An accreditation review process developed for U.S.-based high and maximum containment research facilities could, like the CEN standard, include an evaluation to

[176] For more information about the European Committee for Standardization (Comité Européen de Normalisation or CEN), see www.cen.eu. The final version of the CEN publication, *Laboratory Biorisk Management Standard* (CWA 15793), is available at http://www.cen.eu/cenorm/sectors/technicalcommitteesworkshops/workshops/ws31.asp.

determine whether a facility meets the requirements for managing its biohazard risks as established by the accrediting organization. The lack of a formal accreditation or re-accreditation program for all institutional biosafety management programs at U.S. institutions with high or maximum containment laboratories has been discussed at meetings of the American Biological Safety Association (ABSA).[177] ABSA has developed a position paper on accreditation. [178]

A decision to require laboratory accreditation would need to be accompanied by clear national standards that biosafety/biocontainment management systems should meet, and an indication of what entity (entities) would serve as an accrediting body.[179] A feasibility study of the issue of accreditation could be undertaken by a representative group of Federal and non-Federal stakeholders. Another possible approach is to establish requirements for Approved Accrediting Organizations (AAO). This approach is used by HHS Centers for Medicare and Medicaid Services (CMS) to accredit healthcare organizations, laboratories, and ambulatory care facilities, etc., as Medicare providers.

It should be noted that the terminology used to describe accreditation can differ from one organization to another. Some organizations refer instead to laboratory "certification" as encompassing the review and approval processes required before a laboratory can begin operation, or for a laboratory to remain in operation. NIH, for example, uses the term certification (rather than accreditation) to refer to the requirements and processes developed for the review of its intramural high and maximum containment laboratories. The NIH "Biosafety Level 3-Laboratory Certification Requirements" provide for "the systematic review of all safety features and processes associated with the laboratory (engineering controls, personal protective equipment, building and system integrity, standard operating procedures, and administrative controls such as documentation and record retention systems)."[180]

In this context, the NIH intramural laboratory certification program resembles that defined by the World Health Organization (WHO) in the *WHO Laboratory Biosafety Manual – Third Edition 2004*.[181] The WHO manual indicates that laboratory certification is "the systematic examination of all safety features and processes within the laboratory (engineering controls, personal protective equipment and administrative controls).

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[177] *Biosafety on the Horizon*, 51st Annual Biological Safety Conference, American Biological Safety Association, October 2008.

[178] The American Biological Safety Association position paper, *Accreditation of High Containment Laboratories* (April 2008), is available at http://www.absa.org/pdf/080418contlabs.pdf.

[179] An accrediting body could be a non-Federal, third-party agent such as a professional organization or society.

[180] For more information about the NIH "Biosafety Level 3-Laboratory Certification Requirements," see at http://dohs.ors.od.nih.gov/pdf/BSL3%20CertificationRequirements-FINAL.pdf.

[181] The *WHO Laboratory Biosafety Manual – Third Edition 2004* is available at http://www.who.int/csr/resources/publications/biosafety/Biosafety7.pdf. The NIH requirements are more precise with regard to the standards that must be met including actual validation of engineering and HVAC controls. Certification of intramural high-containment laboratories at NIH is performed by a team of professionals with experience and credentials in engineering and biosafety/occupational safety and health.

Biosafety practices and procedures are also examined. Laboratory certification is an ongoing quality and safety assurance activity that should take place on a regular basis."

According to the WHO laboratory manual, "laboratory certification helps to ensure that:

- Proper engineering controls are being used and are functioning adequately as designed
- Appropriate site and protocol specific administrative controls are in place
- Personal protective equipment is appropriate for the tasks being performed
- Decontamination of waste and materials has been adequately considered and proper waste management procedures are in place
- Proper procedures for general laboratory safety, including physical, electrical and chemical safety are in place."

APPENDIX H

Available Training and Certification Programs

As interest in infectious diseases and public health research blossomed in the late 1970's, Dr. Byron Tepper, former Director of the Office of Safety and Environmental Health of The Johns Hopkins University and The Johns Hopkins Hospital, was credited with developing a comprehensive biosafety course entitled *Control of Biohazards in the Research Laboratory*, first offered in 1979 and continuing today. Currently, various academic institutions have developed training programs for students interested in microbiology-related research, which in some cases may include information on biosafety. Also, Federal agencies, professional organizations, and other entities (in addition to individual research institutions) offer training or professional certification programs for individuals who work in high or maximum containment research laboratories. Examples of these training and certification programs include the following.

- Biosafety Professionals
  - The American Biological Safety Association (ABSA) offers training and certification programs, such as those for Certified Biological Safety Professionals and Registered Biosafety Professionals.[182] The programs are designed for biosafety professionals who include microbiologists, biologists, molecular biologists, environmental health scientists, industrial hygienists, clinical health care professionals, veterinarians, chemists and engineers.
  - Through the NBBTP, the National Institute of Allergy and Infectious Diseases (NIAID) and the NIH Division of Occupational Health and Safety (DOHS) have collaborated to prepare research professionals to work in high and maximum containment laboratories. The NBBTP is a post-baccalaureate program managed by a non-profit education and research foundation.[183] Initially established as a 2-year biosafety training fellowship, the program was expanded in 2006 to leverage the Federal investment to train more biosafety professionals and to provide specialized training to biocontainment laboratory operations and maintenance personnel through professional development courses and certification programs. The NBBTP is an authorized provider of continuing education units (CEUs) of the International Association for Continuing Education and Training (IACET/ANSI) and is funded through 2011.

- PIs and laboratory scientists

[182] For information about ABSA, see http://www.absa.org/. For information about ABSA certification and registration programs for biosafety professionals, see http://www.absa.org/biocert.html and http://www.absa.org/bioreg.html, respectively.
certification programs, see http://www.absa.org/ and http://www.absa.org/biosafety.html.
[183] For more information about the NBBTP, see http://www.nbbtp.org/nf_home.cfm.

- In 2007, NIH and the World Health Organization (WHO) collaborated to prepare the 2nd Edition of *An Instructor's Guide to Biosafety Training*.[184]
- Recently, the NIH intramural program has dedicated the NIH Maximum Containment Laboratory (MCL) in Bethesda, Maryland, to training personnel in safe BSL-4 operations. The MCL will become a national BSL-4 training center, and arrangements for training can be made to include non-Federal employees. Three curriculum tracks are under development to train research personnel, animal care technicians, and animal husbandry personnel in safe BSL-4 operations. This facility complements the NIH BSL-3 mobile training facility located on the NIH campus. Considerable resources have been allocated to ensure that adequate biosafety training opportunities are available to support the biocontainment laboratory infrastructure expansion.
- Originally developed and funded by the NIH and previously known as the Johns Hopkins Biosafety course, the course entitled "Control of Biohazards in the Research Laboratory" is a 4½-day program designed for participants with or without previous biosafety experience.[185]
- The Midwest Regional Center of Excellence offers the "Biosafety for the Research Scientist Course" for post-doctoral scientists, including microbiologists, clinicians, researchers from other disciplines, and scientists in biodefense or emerging infectious diseases research (from academic, government, and private industry laboratories).[186]
- Training programs are offered by the Southeastern Regional Center of Excellence for Emerging Infections and Biodefense (SERCEB)[187] and the Eagleson Institute.[188] SERCEB has collaborated with the Center for Public Health Preparedness and Research to develop an education and training program in BSL-2, BSL-3, and BSL-4 laboratory safety practices that is conducted in a mock BSL-3/4 laboratory at Emory University.[189]
- Sandia National Laboratories, in partnership with Frontline Foundation of Atlanta, Georgia, offers a course entitled Controlling Laboratory Biorisks, which covers the foundations of laboratory biosafety and biosecurity.[190]
- The Biosafety and Biosecurity Training Course (BBTC) is offered annually at the Colorado State University, Fort Collins. It includes 2½ days of instruction about large animal, small animal, and primate Animal

[184] The NIH/WHO manual entitled *An Instructor's Guide to Biosafety Training* is available at http://apbtn.com/apbtn/trainingMaterials.html.
[185] For more information about the "Control of Biohazards in the Research Laboratory" course, see http://www.controlofbiohazards.com/.
[186] For more information about the Biosafety for the Research Scientist Course, see http://mrce.wustl.edu/index.php?id=dynamic_page&itemid=60.
[187] SERCEB Career Development for Basic Scientists in Emerging Infections and Biodefense. See http://www.serceb.org/about_biosafetytraining.htm.
[188] For more information about Eagleson Institute: Training and Resources, see http://www.bakerco.com/resources/eagleson.php.
[189] Biosafety courses for laboratory staff of BSL-2, BSL-3, and BSL-4 facilities are offered through Emory University. For more information, see http://www.sph.emory.edu/CPHPR/biosafetytraining/index.html.
[190] For more information about the training course offered by Sandia, see http://www.frontlinefoundation.org/ncp_home.cfm.

Biosafety Level-2 (ABSL-2) and ABSL-3 containment design and procedures, and 2 days of instruction about plant biosafety and containment.[191]

- The National Registry of Certified Microbiologists (NRCM) certifies professional microbiologists at the pre-baccalaureate/post-baccalaureate, master's, and doctoral levels to promote the high-quality practice of microbiology and minimize risk to the public.[192] A comprehensive biosafety course entitled *Control of Biohazards in the Research Laboratory*, first offered in 1979 and continuing today, is designed to prepare individuals planning to take the NCRM exam, and for individuals applying to ABSA for training as a Registered Biological Safety Professional or Certified Biological Safety Professional.

- Animal care and veterinary staff. The American Association for Laboratory Animal Science (AALAS) certifies three levels of technician competence.[193] The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International's Education and Outreach Program is designed to help institutions "achieve and sustain Full Accreditation by providing topical education and outreach services based on the AAALAC International perspective."[194] Other courses are under development.[195]

- Maintenance and cleaning staff. A training program for high and maximum containment laboratory operations and maintenance personnel is the NBBTP at NIH. There are two curriculum tracks, Operations and Maintenance or Biosafety and Biocontainment.[196]

[191] For more information about the Biosafety and Biosecurity Training Course, see http://www.cvmbs.colostate.edu/mip/crwad/BBTC.htm.
[192] For more information about the ASM NRCM certification programs, see http://www.asm.org/Academy/index.asp?bid=2250.
[193] For more information about AALAS certification programs, see http://www.aalas.org/Certification/tech_cert.asp.
[194] For more information about the educational programs offered by AAALAC, see http://www.aaalac.org/education/index.cfm.
[195] A curriculum for animal care technicians and veterinary staff, and animal husbandry personnel working in BSL-4 environments is under development at the NIH. Also, AALAS is developing training curricula for individuals who work in ABSL-3 and ABSL-4 facilities.
[196] Information excerpted from the NBBTP website. For more information about the NBBTP, see http://www.nbbtp.org/ncp_home.cfm.

APPENDIX I

Proposed Centralized Incident-Reporting, Analysis, and Information-Sharing System

Prompt and detailed reporting of significant laboratory incidents (accidents, laboratory-acquired infections [LAIs], significant exposures, etc.) involving high or maximum containment research is another component of comprehensive and effective biosafety and biocontainment oversight. An analysis of reports of laboratory incidents could help improve laboratory safety and oversight, determine why the incidents occurred and how they can be prevented in the future, provide a resource for generating and sharing lessons learned, and point to the need for new or revised guidelines, practices, or training (see Objective 4).

The Trans-Federal Task Force on Biosafety and Biocontainment Oversight (Task Force) recommends the establishment of a voluntary, non-punitive centralized system for incident-reporting, analysis, and information-sharing across all high and maximum containment research laboratories in all sectors that would ensure the protection of sensitive and private information, as necessary. In addition to the considerations identified in Chapter VII of this report, its establishment would include efforts to develop:

- A clear, consistently applied definition of what constitutes an incident that should be reported, and methods to determine whether an infection was acquired in the laboratory

- Specific guidance for reporting incidents related to research on non-select agents, non-agricultural agents, and non-recombinant DNA (rDNA) agents

- A clear description of the entity that would be responsible for establishing and operating a centralized incident-reporting system, how the data would be analyzed and shared, what additional authorities might be needed, etc.

- An evaluation of model systems for incident reporting, including the *Report-LAI* system under development by the NIH and CDC, and the no-fault, centralized incident-reporting system used by the Federal Aviation Administration (FAA)[197]

- The development of effective ways to encourage physicians to consider whether an infection in a patient could be an uncommon LAI (rather than assuming it is a common illness with similar symptoms)

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

Facility Review and Inspection

Inspections of laboratory facilities help ensure overall safety and compliance with applicable biosafety and biocontainment regulations, guidelines, standards, and policies. Inspections are conducted to ensure that all workers 1) are aware of the risks associated with the work in the laboratory, including animal, physical, biological, and chemical hazards; 2) are trained on how to mitigate those risks through the appropriate use of engineering controls, safe work practices, and protective equipment; 3) comply with regulatory requirements, such as those pertaining to bloodborne pathogens or other infectious materials, and storage, handling, and disposal of hazardous materials; and 4) comply with required security measures. Inspections also help determine whether facility design and protective equipment are appropriate for the work being conducted, and whether the maintenance of facility infrastructure and equipment is sufficient.

Currently, all entities that possess, use, or transfer select agents must register with the Select Agent Program and participate in inspections conducted by the HHS Centers for Disease control and Prevention (CDC) and/or the USDA Animal and Plant Health Inspection Service (APHIS). Under the *Select Agent Regulations*, CDC and/or APHIS inspections are required every 3 years and occur in addition to the annual self-inspections required of regulated entities. The shipping and handling facilities of entities that transfer select agents may be inspected by the Department of Transportation (DOT), particularly if they handle high volumes of shipments. In addition, entities that receive funds from the National Institutes of Health (NIH) for recombinant DNA research must comply with the *NIH Guidelines for Research Involving Recombinant DNA Molecules*, and may be asked to participate in a site visit by the NIH Office of Biotechnology Activities (OBA).

Also, depending upon their organizational affiliation, entities that possess, use, or transfer select agents may undergo additional inspections. For example, Federal agencies such as CDC, NIH, and the USDA Agricultural Research Service (ARS) have internal safety offices that may perform inspections in addition to those required under the *Select Agent Regulations*. The criteria related to these internal inspections can be more "prescriptive" than "performance-driven" inspection criteria associated with the Select Agent Program.

A facility review or inspection could include (but is not limited to) evaluation of:

- Biosafety management and business programs. Examples include:
    - Business and administrative processes, policies, and resources
    - Safety management officials and responsibilities
    - Safety committees, safety manuals, standard operating procedures (SOPs), internal inspections, etc.
    - Record-keeping, including inventory of agents

- Employee expertise, training, and documentation

- Occupational health programs
  - Exposure monitoring
  - Employee medical surveillance programs (e.g., medical history, vaccination, titers, and respiratory protection)
  - Pre-exposure programs and policies
  - First aid and post-exposure programs
  - Medical treatment and followup
  - Documentation of accidents, injuries, incidents, and followup

- Biosafety programs, including those pertaining to:
  - Facilities
  - Laboratory equipment and maintenance
  - Personal protective equipment
  - Employee safety practices and procedures
  - Documentation of accidents, incidents, injuries and follow-up actions
  - Agent storage and repositories

- Waste management programs

- Chemical management programs

- Biosecurity programs (protection of agents, personnel reliability, physical security, etc.)

- Emergency response programs, including emergency action plan, fire drill, shelter-in-place, etc.

- Packaging and shipping of infectious substances