Guiding Principles for Biosafety Governance:

Ensuring Institutional Compliance with Biosafety, Biocontainment, and Laboratory Biosecurity Regulations and Guidelines

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Prepared on behalf of the Federal Experts Security Advisory Panel
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A. Introduction

In July 2010, the Federal Experts Security Advisory Panel (FESAP) was established by Executive Order 13546[1] to provide recommendations related to the security of biological select agents and toxins (BSAT) to the Secretaries of Health and Human Services and Agriculture and the Attorney General. In July 2014, the FESAP was re-chartered to evaluate approaches to enhance biosafety and biosecurity in the United States.

In response to incidents involving BSAT that raised safety and security issues, in September 2014, the White House National Security Council (NSC) tasked the FESAP to 1) identify needs and gaps and make recommendations to optimize biosafety, biosecurity, oversight, and inventory management and control for BSAT; 2) identify actions and any regulatory changes to improve biosafety and biosecurity; and 3) identify an approach to determine the appropriate number of high-containment U.S. laboratories required to possess, use, or transfer BSAT. Recommendations were finalized in the Report of the Federal Experts Security Advisory Panel dated December 2014[2]. The United States Government (USG) has developed a plan[3] to implement the FESAP's recommended actions with the expectation that implementing the recommended actions will strengthen biosafety and biosecurity practices and oversight activities.

FESAP Recommendation 1.2[4] was to require that all research institutions, in which human, plant, and/or animal infectious agents and toxins research is conducted, have an appropriate organizational and governance structure to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines. Given the importance of ensuring institutions have robust and comprehensive governance structures in place for the oversight of biosafety and biosecurity, the USG has developed the following guidance document on biosafety and biosecurity governance. This document provides a number of guiding principles and best practices for ensuring institutions have appropriate organizational and governance structures in place to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines. This document also provides an overview of the Federal regulations, requirements, and guidelines that pertain to biosafety and biosecurity in the U.S. and a description of some of the voluntary laboratory accreditation systems and other standards that relate to, or incorporate, biosafety and biosecurity oversight. Finally, this

[1] https://www.gpo.gov/fdsys/pkg/FR-2010-07-08/pdf/2010-16864.pdf
[2] http://www.phe.gov/Preparedness/legal/boards/fesap/Pages/default.aspx
[3] http://www.phe.gov/s3/Documents/fesap-ftac-ip.pdf
[4] http://www.phe.gov/s3/Documents/fesap.pdf

document provides a description of the biosafety and biosecurity oversight frameworks that are in place at the institutional level for ensuring compliance with federal requirements and guidelines.

B. Biosafety, Biocontainment and Biosecurity Governance Structure in the U.S.

The United States has a comprehensive biosafety, biocontainment, and biosecurity oversight system designed to protect laboratory workers, public health, agriculture, the environment, and national security. Biosafety and biocontainment oversight rests on a foundation of federal regulations, guidelines, and policies and is provided at multiple levels (See Figure 1). Oversight of day to day research activities is largely a responsibility of the institutions and the investigators conducting the research with direct biosafety oversight being implemented at the local level.

Figure 1 – Biosafety and Biosecurity Oversight Framework

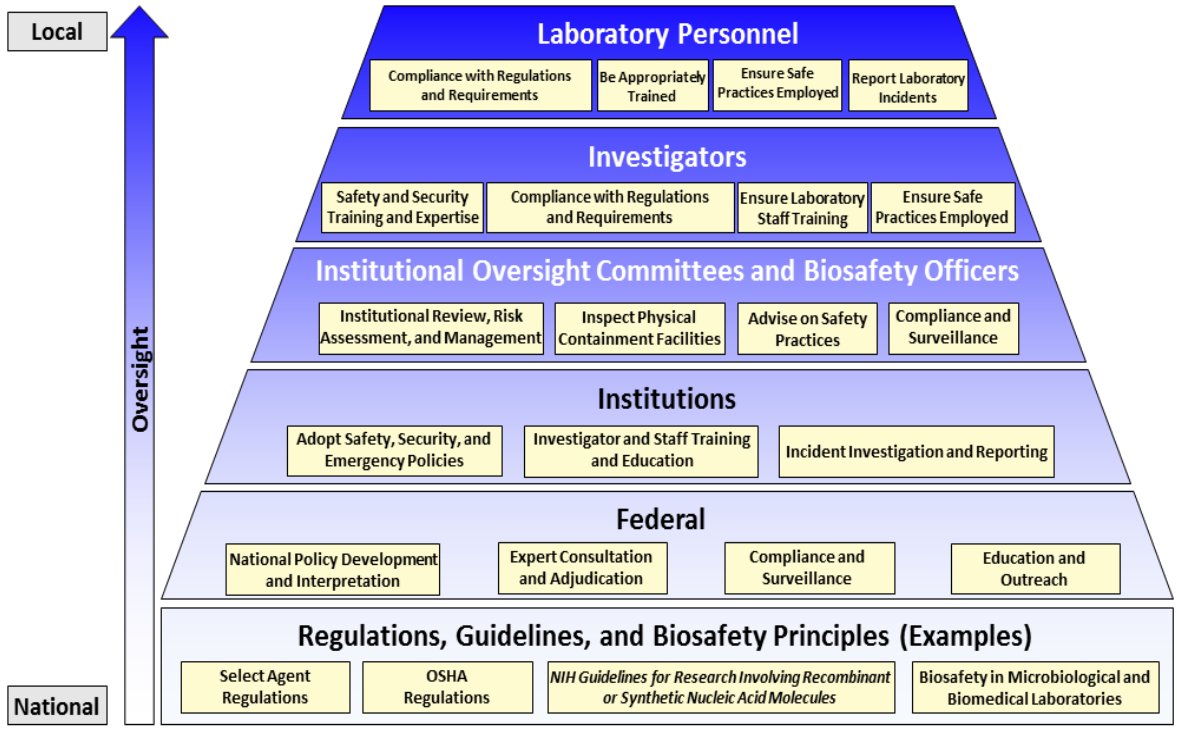

Figure 1. Biosafety and biocontainment oversight rests on a foundation of federal regulations, guidelines, and policies from which multiple levels of oversight are built.

C. Guiding Principles and Best Practices for Ensuring Institutions Have an Appropriate Organizational and Governance Structure to Ensure Compliance with Biosafety, Biocontainment, and Laboratory Biosecurity Regulations and Guidelines

To assist institutions in ensuring compliance with federal requirements and fostering a culture of responsibility for biosafety and biosecurity, the following guiding principles and best practices are offered for consideration. These principles and practices are intended to promote robust programs of oversight and to ensure that all those at the institution who are conducting or overseeing life sciences research are aware of their responsibilities for compliance with biosafety and biosecurity requirements and the importance of upholding a strong culture of biosafety, biosecurity, and responsible conduct within the research community.

Establish formal, written policies and standard operating procedures for biosafety and biosecurity oversight to ensure compliance with Federal regulations and guidelines. Review these policies and standard operating procedures frequently.
Comprehensive written policies and standard operating procedures (SOPs) that have performance expectations clearly stated are key to ensuring that responsibilities and duties are fulfilled consistently. SOPs can also facilitate successful training. Policies and SOPs should be living documents that are reviewed and updated frequently to ensure they remain current and relevant, and address compliance with all applicable requirements and standards.

Articulate the roles and responsibilities of all individuals conducting or overseeing life sciences research for ensuring compliance with biosafety and biosecurity requirements, including senior administrators, oversight committees, principal investigators, laboratory personnel and students.
It is important to clearly state that all relevant individuals at the institution have a role and responsibility for ensuring adherence to biosafety and biosecurity requirements and standards.

Conduct regular assessments of committees, offices, and departments with responsibilities for biosafety and biosecurity oversight to assess their function and strengthen their performance when necessary.
Periodic self-assessment is an important component of maintaining the quality of institutional programs of biosafety and biosecurity. Institutions should frequently assess the performance of compliance committees and departments and offices that have responsibilities for implementing and overseeing biosafety and biosecurity policies to

ensure they are functioning optimally. An IBC Self-Assessment Tool is available on the NIH Office of Science Policy website[5]. There should also be formal systems for performance evaluation, benchmarking, and reporting to institutional leadership.

Coordinate activities among committees, departments, offices, and staff with biosafety and biosecurity oversight and compliance responsibilities.

Coordination and collaboration among entities responsible for biosafety and biosecurity oversight can help to promote compliance. While the purview and specific responsibilities of research oversight committees are generally distinct, they often overlap in the research they oversee. For example the Institutional Biosafety Committee (IBC) and Institutional Animal Care and Use Committee (IACUC) both review and approve research with animals and biohazards associated with animal research. Strategies for coordination may include having common members on committees, strong lines of communication between departments and staff supporting various compliance activities, joint databases, and coordinated protocol reviews.

Ensure the institution has a robust mandatory training program for all personnel working with biohazardous materials.

Training programs should not only cover the requirements articulated in federal biosafety and biosecurity regulations and guidelines, but also aim to promote and enhance a culture of safety within the community. Training programs ideally consider not only provision of information (e.g. classroom presentations) but hands-on learning, mentorship, and (ideally independent) performance verification.

Ensure senior leadership is engaged with respect to institutional biosafety and biosecurity oversight and compliance functions.

Promoting a safety and security culture involves both top-down and bottom-up approaches. It is vital that the highest levels of institutional leadership convey their commitment to safety and security and their importance to the institution.

Ensure appropriate resources are devoted to biosafety and biosecurity oversight and compliance activities at the institution.

Senior institutional officials should commit to providing adequate support (material and staffing, capital planning for facilities maintenance or enhancement, etc.) to ensure the operational aspects of the biosafety and biosecurity programs can function optimally. Needs should be periodically evaluated to ensure that all biosafety and biosecurity program elements (inspections, training, safety equipment maintenance, facilities performance, etc.) have the necessary resources.

[5] https://osp.od.nih.gov/biotechnology/nih-guidelines/

Promote transparency regarding institutional biosafety and biosecurity oversight.
Transparency should be promoted within the institution to clearly articulate to the members of the research community their responsibilities and the expectations that the institution regarding compliance with biosafety and biosecurity requirements. The institution should also be transparent to the external community about its oversight systems and safety culture. This will ensure the institution is publically accountable and also promotes public trust in the safety of the research enterprise.

Foster a culture of responsibility regarding biosafety and biosecurity among all personnel overseeing or conducting work with biohazardous materials at the institution.
The institution should foster a culture of responsibility within the research community by educating and raising awareness about the importance of biosafety and biosecurity, and clearly stating institutional expectations for behaviors that promote biosafety and biosecurity. Biosafety and biosecurity should be core institutional values championed by institutional leadership and be seen as an important component of responsible conduct of research.

D. Federal Biosafety and Biosecurity Regulations and Guidelines

The federal regulations that pertain most directly to biosafety and biosecurity oversight at laboratories in the U.S. are the Select Agent Regulations (SAR), Occupational Health and Safety Administration (OSHA) regulations, and the permitting regulations of the United States Department of Agriculture (USDA) and the Centers for Disease Control and Prevention (CDC). Other regulations include the Department of Transportation (DOT) regulations for shipping biological materials and the Department of Commerce (DOC) regulations related to export control. A number of other policies and guidelines also articulate requirements for biosafety and biosecurity oversight at institutions conducting research with biological materials.

1. Policies and Guidelines on the Conduct of Research

National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)[6]

The *NIH Guidelines*, administered by the NIH Office of Science Policy (OSP), specify scientifically-based practices for the safe construct and handling of recombinant or synthetic nucleic acid molecules, and cells, organisms and viruses containing such molecules. The *NIH Guidelines* also include information on biosafety and biocontainment requirements for human subjects, animals, and insects participating or used in research involving recombinant/synthetic organisms. Institutions subject to the *NIH Guidelines* must establish and implement policies that provide for the safe conduct of research, and ensure compliance with the *NIH Guidelines*. The *NIH Guidelines* also articulate the responsibilities of institutions, investigators, and Institutional Biosafety Committees (IBCs) for biosafety oversight.

[6] https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf

The IBCs are the locus of oversight for the research subject to the *NIH Guidelines* at the institutional level and have responsibilities including:

- Reviewing and approving research with recombinant or synthetic nucleic acid molecules
- Assessing the facilities, procedures and practices, and appropriate biosafety containment levels for the research
- Periodically reviewing research to ensure compliance with biosafety requirements
- Ensuring appropriate training for laboratory personnel
- Implementing health surveillance programs as necessary
- Adopting emergency plans addressing accidents and incidents such as spills and personnel contamination

The *NIH Guidelines* are a term and condition of funding for all institutions that receive any support for recombinant or synthetic nucleic acid molecule research from the NIH. Some other federal agencies may also require compliance with the *NIH Guidelines* as a term and condition of their own funding.

Recommended Policy Guidance for Departmental Development of Review Mechanism for Potential Pandemic Pathogen Care and Oversight[7]

The Office of Science and Technology Policy (OSTP) has issued guidance to Federal departments and agencies for the establishment of review and reporting processes to inform federal funding decisions and strengthen oversight for proposed research that may be anticipated to create, transfer, or use enhanced potential pandemic pathogens. The policy guidance instructs Federal departments and agencies to adopt an appropriate review and oversight mechanism in order to consider conducting or funding such research.

United States Government Policies on Life Sciences Dual Use Research of Concern

Despite the value and benefits of life science research to public health and safety, certain types of research conducted for legitimate purposes can be utilized for both benevolent and harmful purposes. Such research is called “dual use research.” Dual use research of concern (DURC) is a subset of dual use research defined as life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

Recognizing the potential risks of DURC, the United States Government issued two complementary polices aimed at sharing responsibility between federal funders of life science research and the institutions who conduct such research. The policies call for establishing a mechanism to review life science research in order to identify DURC and, if necessary, developing risk mitigation strategies to reduce any potential risk of misuse.

[7] https://www.phe.gov/s3/dualuse/Documents/P3CO-FinalGuidanceStatement.pdf

The United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern[8] sets forth a process of regular federal review of U.S. government-funded or conducted research and requires federal agencies that fund or conduct life sciences research to identify DURC and evaluate this research for possible risks, as well as benefits, and to ensure that risks are appropriately managed and benefits realized.

The United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern[9] applies to institutions receiving federal funds that conduct or sponsor life sciences research with the agents or toxins listed in the policy. The policy requires institutions to establish an Institutional Review Entity (IRE) to review research for experiments that may involve DURC, to perform a risk/benefit analysis, and to implement appropriate risk mitigation measures.

Tools for the Identification, Assessment, Management, and Responsible Communication of Dual Use Research of Concern[10]
A companion guide to the United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern, entitled *Tools for the Identification, Assessment, Management, and Responsible Communication of Dual Use Research of Concern*, was developed to assist institutions, investigators, and IREs in the development of policies and practices for the effective oversight of DURC and in the execution of some of the required steps for institutional review and oversight.

2. Select Agent Regulations (SAR)

The U.S. Departments of Health and Human Services (HHS) and Agriculture (USDA) regulations for the possession, use, and transfer of select agents and toxins (42 CFR Part 73[11]**, 7 CFR Part 331**[12]**, and 9 CFR Part 121**[13]**)**
The SAR cover the possession, use and transfer of certain biological agents and toxins that have the potential to pose a severe threat to public, animal or plant health or to animal or plant products. The authority for the SAR is the Public Health Security and Bioterrorism Preparedness and Response Act of 2002[14]. The SAR require individuals or entities that possess, use, or transfer BSAT to register with either HHS or USDA under the FSAP.

All registered individuals and entities are required by the SAR to have a biosafety plan, a security plan, and an incidence response plan. The FSAP monitors compliance with the SAR through an inspection program. FSAP assessments allow inspectors to ensure that appropriate biosafety and security measures are in place, as well as ensure that laboratory workers are

[8] http://www.phe.gov/s3/dualuse/Pages/USGOversightPolicy.aspx
[9] http://www.phe.gov/s3/dualuse/Pages/InstitutionalOversight.aspx
[10] http://www.phe.gov/s3/dualuse/Pages/companion-guide.aspx
[11] http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title42/42cfr73_main_02.tpl
[12] http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title07/7cfr331_main_02.tpl
[13] http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title09/9cfr121_main_02.tpl
[14] https://www.gpo.gov/fdsys/pkg/PLAW-107publ188/pdf/PLAW-107publ188.pdf

adequately trained. The SAR also require the reporting of incidents of theft, loss and release of BSAT to the FSAP.

Individuals must undergo a security risk assessment (SRA) conducted by the Federal Bureau of Investigation (FBI) prior to being granted access to BSAT. Those individuals identified by the FBI as a "restricted person" are prohibited from access to BSAT (see 18 USC §175b[15]). This SRA is repeated every three years by the FBI. A subset of select agents and toxins have been designated as Tier 1 because these biological agents and toxins present the greatest risk of deliberate misuse with significant potential for mass casualties or devastating effect to the economy, critical infrastructure, or public confidence, and pose a severe threat to public health and safety. Individuals who will have access to Tier 1 BSAT are required to be enrolled in the entity's suitability assessment program[16] which includes a pre-access suitability assessment and an ongoing suitability assessment. The purpose of a pre-access assessment is to determine if an individual displays behaviors (as determined by the registered entity) that would increase the risk of a theft, loss, or release of a select agent or toxin. After suitability for working with select agents is determined though the initial pre-access suitability assessment, ongoing suitability assessments ensure that an approved individual maintains continued suitability for working with BSAT.

3. Biosafety and Workplace Safety

Biosafety in Microbiological and Biomedical Laboratories[17]

Biosafety in Microbiological and Biomedical Laboratories (BMBL) is a guidance document developed by the CDC and the NIH. Currently in its fifth edition, the BMBL provides guidance on protecting laboratory workers and the public from exposure to infectious biological materials and regulated biological toxins that pose various levels of risk to human health, and the containment of biological hazards within the laboratory. The BMBL has become the code of practice, authoritative reference, and de facto standard of operations for U.S. laboratory biosafety and biocontainment principles, practices, and procedures. Adhering to the BMBL is a requirement for entities in receipt of funding from HHS for certain research grants and contracts, in accordance with 42 CFR 52[18], Grants for Research Institutes. The Department of Homeland Security (DHS) also requires entities performing life sciences research that is conducted, funded, or sponsored by DHS to adopt and implement the latest edition of the BMBL, in accordance with its Management Directive 066-02, Biosafety[19].

[15] https://www.gpo.gov/fdsys/granule/USCODE-2002-title18/USCODE-2002-title18-partI-chap10-sec175b
[16] https://www.selectagents.gov/resources/Suitability_Guidance.pdf
[17] https://www.cdc.gov/biosafety/publications/bmbl5/index.htm
[18] https://www.ecfr.gov/cgi-bin/text-idx?SID=09cc241267ac08a43e669fddddb006c6&mc=true&node=pt42.1.52&rgn=div5
[19] https://www.dhs.gov/sites/default/files/publications/17_0713_Directive%20066-02_Rev%2001_Biosafety_0.pdf

Occupational Safety and Health Administration Requirements

With the Occupational Safety and Health (OSH) Act of 1970, Congress created OSHA to assure safe and healthful working conditions for working men and women, including by setting and enforcing standards. OSHA has oversight authority for the safety and health of workers in all workplaces that fall under its jurisdiction, including individuals who work with biological agents or toxins in containment facilities. Regulations promulgated to implement the OSH Act and protect worker safety and health include:

- **Bloodborne Pathogens standard (29 CFR 1910.1030[20])**
- **Personal Protective Equipment (PPE) standard (29 CFR 1910.132[21])**
- **Eye and Face Protection standard (29 CFR 1910.133[22])**
- **Respiratory Protection Standard (29 CFR Part 1910.134[23])**
- **Foot Protection standard (29 CFR 1910.136[24])**
- **Hand Protection standard (29 CFR 1910.138[25])**
- **Occupational Exposure to Hazardous Chemicals in Laboratories (29 CFR 1910.1450[26])**
- **Hazardous Waste Operations and Emergency Response (HAZWOPER) standard (29 CFR 1910.120[27])**

Depending on the hazards present or reasonably anticipated to be present in the laboratory environment, these and other standards may apply.

Under the General Duty Clause, Section 5(a)(1) of the OSH Act, employers are required to provide their employees with a place of employment that is "free from recognized hazards that are causing or are likely to cause death or serious harm" to employees.

4. Agricultural Regulations and Animal Care and Use Guidelines

USDA Animal Plant Health Inspection Service (APHIS) Permitting Regulations (9 CFR 122[28], 7 CFR 330[29] and 340[30])

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[20] http://www.ecfr.gov/cgi-bin/text-idx?SID=46ad27b0a0312ec26d4908f47c082b67&mc=true&node=se29.6.1910_11030&rgn=div8

[21] http://www.ecfr.gov/cgi-bin/text-idx?rgn=div6&node=29:5.1.1.1.8.9

[22] https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=9d2df24790bd9574b7d239ccb1681187&ty=HTML&h=L&mc=true&n=pt29.5.1910&r=PART#se29.5.1910_1133

[23] http://www.ecfr.gov/cgi-bin/text-idx?SID=6b29026a5dacdce605c7b3993a455e50&mc=true&node=se29.5.1910_1134&rgn=div8

[24] https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=9d2df24790bd9574b7d239ccb1681187&ty=HTML&h=L&mc=true&n=pt29.5.1910&r=PART#se29.5.1910_1136

[25] https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=1&SID=9d2df24790bd9574b7d239ccb1681187&ty=HTML&h=L&mc=true&n=pt29.5.1910&r=PART#se29.5.1910_1138

[26] https://www.ecfr.gov/cgi-bin/text-idx?SID=6bc767478e5dcda5d0a7ecdb91c13f6a&mc=true&node=se29.6.1910_11450&rgn=div8

[27] https://www.ecfr.gov/cgi-bin/text-idx?node=29:5.1.1.1.8.8.33.14

[28] http://www.ecfr.gov/cgi-bin/text-idx?SID=ba7fca277d84a212d8d5de68ed94ea7a&node=9:1.0.1.5.59&rgn=div5

Through its permitting system, APHIS regulates the transport and use of agents that are hazardous to agriculture including certain livestock, poultry, and crop pathogens. APHIS inspects facilities to ensure they provide adequate containment of regulated agricultural agents.

Guide for the Care and Use of Laboratory Animals[31]

Institutions receiving funding through the Public Health Service (PHS) or National Science Foundation (NSF) are required to establish an assurance with the NIH Office of Laboratory Animal Welfare[32] (OLAW) and comply with PHS Policy on Humane Care and Use of Laboratory Animals, through standards articulated in the National Research Council's publication titled "Guide for the Care and Use of Laboratory Animals," 8th edition. Sections of the Guide specifically address expectations for institutional occupational health programs and animal biosecurity and hazardous agent containment, including biological agents.

Arthropod Containment Guidelines[33]

Referenced in Appendix E of the BMBL, the Arthropod Containment Guidelines (ACG) were developed by members of the American Committee on Medical Entomology (ACME), a subcommittee of the American Society of Tropical Medicine and Hygiene (ASTMH). Risk assessment principles for research on arthropods of public health importance are outlined for the IBC to establish an appropriate arthropod containment level (ACL 1-4). For each ACL, guidance is provided for standard practices, special practices, safety equipment and facilities.

5. Environmental Regulations

Resource Conservation and Recovery Act[34]

The Resource Conservation and Recovery Act (RCRA) requires that all wastes be managed in a manner which minimizes harm to human health and the environment. Many states are authorized or approved to administer the RCRA programs and to ensure compliance, and states may regulate solid and hazardous wastes under their own authorities as well. The state regulations must be as stringent as the federal regulations but may also be more stringent or broader in scope than federal regulations. Most if not all states require that hazardous biological agents be either destroyed or inactivated on site before disposal as solid waste, or packaged as regulated medical waste, or handled as a special Category A infectious substance and transferred to a licensed third party for decontamination via autoclaving or incineration.

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[29] http://www.ecfr.gov/cgi-bin/text-idx?SID=d403c0d8c205fbeb13cc4d7f8ba532d4&mc=true&node=pt7.5.330&rgn=div5

[30] http://www.ecfr.gov/cgi-bin/text-idx?SID=d403c0d8c205fbeb13cc4d7f8ba532d4&mc=true&node=pt7.5.340&rgn=div5

[31] https://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-use-of-laboratory-animals.pdf

[32] http://grants.nih.gov/grants/olaw/olaw.htm

[33] https://www.cdc.gov/biosafety/publications/bmbl5/bmbl5_appendixe.pdf#x2013; Arthropod Containment Guidelines (ACG) [PDF - 207 KB]

[34] https://www.epa.gov/laws-regulations/summary-resource-conservation-and-recovery-act

6. Transportation and Import/Export Regulations

Department of Transportation (DOT) Hazardous Materials Regulations (49 CFR 171-180[35])
The transportation of infectious substances is regulated by the DOT Hazardous Materials Regulations. These regulations detail specific measures to ensure that infectious substances are shipped safely, and articulate the requirements for the transportation of infectious substances including cover packaging, marking, labelling, documentation, security, and incident reporting.

HHS CDC Import Permit Regulations (42 CFR Section 71.54[36])
Permits are required for the import of infectious biological agents, infectious substances, and vectors of human disease into the United States, excluding those items listed under 42 CFR 71.54(f) (i.e. select agents listed in 42 CFR Part 73[37] whose importation has been authorized in accordance with 42 CFR 73.16[38] or 9 CFR 121.16[39]). The regulations require importers to implement biosafety measures commensurate with the hazard posed by the infectious biological agent, infectious substance, and/or vector to be imported, and the level of risk given its intended use.

The Export Administration Regulations (15 CFR 730-774[40])
The Export Administration Regulations (administered by the DOC Bureau of Industrial Security) set the rules for the control of export and re-export of commodities including certain biological materials.

7. Biotechnology Regulations

Coordinated Framework for Regulation of Biotechnology (51 FR 23302[41])
The Coordinated Framework is intended to provide a comprehensive federal regulatory system to ensure the safety of biotechnology research and products. The Coordinated Framework describes the regulatory policies of the Food and Drug Administration (FDA), USDA APHIS, OSHA and the Environmental Protection Agency (EPA) and the research policies of the NIH, EPA, USDA, and National Science Foundation (NSF).

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[35] http://www.ecfr.gov/cgi-bin/text-idx?SID=1dc274f19ef86ae0f2f465dba9ce8697&mc=true&tpl=/ecfrbrowse/Title49/49CIsubchapC.tpl
[36] http://www.ecfr.gov/cgi-bin/text-idx?SID=d403c0d8c205fbeb13cc4d7f8ba532d4&mc=true&node=pt42.1.71&rgn=div5#se42.1.71_154
[37] http://www.ecfr.gov/cgi-bin/text-idx?SID=d403c0d8c205fbeb13cc4d7f8ba532d4&mc=true&node=pt42.1.73&rgn=div5
[38] http://www.ecfr.gov/cgi-bin/text-idx?SID=1ff7f4a39d416cc3c21f85096c064a19&mc=true&node=se42.1.73_116&rgn=div8
[39] http://www.ecfr.gov/cgi-bin/text-idx?SID=d403c0d8c205fbeb13cc4d7f8ba532d4&mc=true&node=pt9.1.121&rgn=div5
[40] http://www.ecfr.gov/cgi-bin/text-idx?SID=1dc274f19ef86ae0f2f465dba9ce8697&mc=true&tpl=/ecfrbrowse/Title15/15CVIIsubchapC.tpl
[41] https://www.epa.gov/sites/production/files/2017-01/documents/2017_coordinated_framework_update.pdf

E. Biosafety Oversight Framework at the Institutional Level

Under the *NIH Guidelines*, all institutions that receive support for research subject to the *NIH Guidelines* are required to establish policies for the safe conduct of such research. A key institutional responsibility is the establishment of an IBC. The IBC is the locus of biosafety oversight at the local level and is responsible for the review and approval of research subject to the *NIH Guidelines*, which includes ensuring appropriate biosafety provisions are in place for the safe conduct of the research. All institutions conducting research subject to the *NIH Guidelines* must register their IBC with the NIH OSP.

IBCs conduct a risk assessment of proposed research with biohazardous materials and infectious agents and develop risk management plans. The IBCs are also responsible for ongoing oversight of the safety of the research, and for ensuring that all laboratory personnel are appropriately trained to conduct the research safely. On behalf of their institutions, the IBCs also adopt institutional safety, security, and emergency response plans. While the *NIH Guidelines* specify that IBCs must have oversight over recombinant and synthetic nucleic acid molecule research, the vast majority of IBCs are charged by their institutions to have a much broader purview, and most also review research with other biohazardous agents at the institution[42].

Under the *NIH Guidelines*, institutions conducting research at high and maximum containment (Biosafety Levels (BSL) 3 and 4) must also appoint a Biological Safety Officer (BSO). The vast majority of institutions registered with NIH OSP have appointed a BSO even if they are only conducting work at lower containment levels. The BSO is responsible for periodic inspections to ensure laboratory safety standards are rigorously followed, providing technical advice to investigators on laboratory biosafety and biosecurity, and developing emergency plans for responding to research related accidents and incidents.

Principal investigators also have a number of biosafety oversight responsibilities for ensuring the safety of the research conducted in the laboratory. Investigators are expected to be knowledgeable about and comply with all biosafety regulations and requirements. They are ultimately responsible for ensuring their laboratory personnel are appropriately trained on working safely with all biological hazards and are employing appropriate biosafety and containment practices to protect the laboratory staff, the public, and the environment.

Other institutional oversight committees are also involved in the governance of life sciences research and their oversight responsibilities may include elements of biosafety and biosecurity. These include Institutional Animal Care and Use Committees (IACUC) and Environmental Health and Safety Committees.

[42] Hackney RW, Jr., Myatt TA, Gilbert K, Caruso RR, Simon SL. Current trends in institutional biosafety committee practices. Applied Biosafety. 2012; 17(1):11–8. Available at: http://journals.sagepub.com/doi/pdf/10.1177/153567601201700103

The IACUC is a governance committee that is responsible for oversight of the institutional animal care and use program and its components as described in the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals and the *Guide for the Care and Use of Laboratory Animals*[43]. The committee reviews research protocols for animal welfare concerns and proposes best practices in the care and use of animals in research laboratories. IACUC responsibilities also include the inspection of animal facilities and programs related to the care and use of animals. IACUC protocols generally include information on any biosafety concerns posed by the animal research, and the IBC and IACUC often coordinate their protocol reviews to ensure the biosafety aspects of the research are managed appropriately. The IACUC reports to the Institutional Official (IO) who is a representative of the senior administration at the institution. The IO makes commitments on behalf of the institution to ensure compliance with the PHS policy.

Many institutions also have additional Environmental Safety and Health Committees. The responsibilities of these committees may include development and review of institutional policies on worker health issues as described by OSHA, including: occupational health, chemical safety, use of personal protective equipment, respiratory protection, radiation, and fire safety.

In addition to the various institutional oversight committees, a number of departments or offices within the institution may have responsibilities for ensuring compliance with regulations and requirements. These may include the environmental health and safety department and research compliance office who may have responsibilities including the development of biosafety and biosecurity policies, the conduct of training on the specific biosafety and biosecurity requirements and responsibilities of personnel conducting life sciences research, and the conduct of inspections to ensure standards and practices are adhered to by research personnel.

F. Dual Use Research of Concern Oversight at the Institutional Level

The USG also has policies in place to promote biosecurity and help ensure that life sciences research information, products, and technologies are not misused to threaten public or agricultural health or national security. Institutions that are in receipt of federal funding for life sciences research are subject to the *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern* and are required to comply with the policy, which describes the organizational framework for review of research with dual use potential and the oversight of DURC. The policy articulates the governance structure that must be in place at institutions for DURC oversight, including the roles and responsibilities of key individuals at the institution.

A key responsibility of the institution is to establish an Institutional Review Entity (IRE). The IRE is charged with the review and oversight of research subject to the policy, including the conduct

[43] https://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-use-of-laboratory-animals.pdf

of risk assessments for research with DURC potential and the development and implementation of risk mitigation plans as appropriate.

The institution must designate an Institutional Contact for Dual Use Research (ICDUR) to serve as an institutional point of contact for questions regarding compliance with and implementation of the requirements for DURC oversight. The ICDUR also serves as the liaison between the institution and the relevant USG funding agencies who also have oversight responsibilities for DURC.

G. Voluntary Laboratory Accreditation Systems and Other Standards Relating To Biosafety and Biosecurity Oversight

In addition to the Federal regulations and guidelines that are in place to ensure that institutions conducting life science research have comprehensive oversight programs in place to ensure compliance with biosafety and biosecurity standards, a number of organizations have developed voluntary accreditation systems and standards to promote best practices which strengthen institutional biosafety and biosecurity programs. Examples of these accreditation programs and voluntary standards are listed below.

1. The American Biological Safety Association (ABSA International)[44]

ABSA administers a voluntary laboratory biosafety accreditation program for BSL-2, Animal Biosafety Level (ABSL)-2, BSL-3 and ABSL-3 laboratories that are not under the jurisdiction of the SAR. Accreditation will provide entities recognition of excellence and compliance with rigorous standards, while providing facilities guidance in generating processes and policies to create a safer environment for their organization, employees, research animals, and the community.

2. AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care International)[45]

Laboratories with animal facilities housing species governed by the Animal Welfare Act[46] (AWA) and may choose to be certified by AAALAC. The accreditation process includes a comprehensive review of animal care and use practices that includes an assessment of the institutional occupational health program and biosafety and biosecurity components.

[44] https://absa.org/
[45] https://www.aaalac.org/
[46] https://www.nal.usda.gov/awic/animal-welfare-act

3. American Association for Laboratory Accreditation[47]

The American Association for Laboratory Accreditation evaluates laboratory safety and security in the context of a broad laboratory quality management system.

4. Clinical Laboratory Improvement Amendments (CLIA)[48]

The Centers for Medicare & Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the U.S. through the CLIA program. The Division of Laboratory Services, within the Survey and Certification Group, under the Center for Clinical Standards and Quality (CCSQ) has the responsibility for implementing the CLIA program. The objective of the CLIA program is to ensure quality laboratory testing. Laboratories with clinical components must comply with CLIA for accreditation purposes. The accreditation process contains both biosafety and biosecurity components.

5. CDC and Association of Public Health Laboratories (APHL) Guidelines

Guidelines for Biosafety Laboratory Competency[49]
These guidelines for biosafety laboratory competency outline the essential skills, knowledge, and abilities required for working with biologic agents at the three highest biosafety levels (BSL 2, 3, and 4). The competencies are tiered to a worker's experience at three levels: entry level, mid level (experienced), and senior level (supervisory or managerial positions).

Competency Guidelines for Public Health Laboratory Professionals[50]
These competency guidelines outline the knowledge, skills, and abilities necessary for public health laboratory (PHL) professionals to deliver the core services of PHLs efficiently and effectively. The domain areas include Security, Emergency Management and Response, General Laboratory Practices, and Safety.

6. ISO 35001: Biorisk Management for Laboratories and Other Related Organizations[51]

The ISO (International Organization for Standardization) 35001 work product is being developed based on content contained within CEN (European Committee for Standardization) Workshop Agreement (CWA) 15793 Laboratory Biorisk Management[52], the first internationally recognized management framework to specifically address hazards associated with biomedical and microbiological laboratories at all biocontainment levels. The CWA 15793 outlines a "plan-do-check-act" systems-oriented management approach to enable an organization to identify,

[47] https://www.a2la.org/appsweb/medical.cfm?fieldpk=17&title=Clinical%20Laboratory%20Accreditation%20Program&certno=0.17&explain=medical
[48] https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/Clia/
[49] https://www.cdc.gov/mmwr/preview/mmwrhtml/su6002a1.htm
[50] http://www.cdc.gov/mmwr/preview/mmwrhtml/su6401a1.htm
[51] http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=66154
[52] https://absa.org/wp-content/uploads/2017/01/CWA15793_Feb2008.pdf

monitor, and control the laboratory biosafety and biosecurity aspects of its operations. As such, CWA 15793 is used by multiple organizations for implementation in diagnostic, clinical and research biomedical laboratories, and for outreach and education on best practices in the laboratory biorisk management process.

Other initiatives that help organizations to promote robust safety programs at the institutional level include a guidance document issued by the Association of Public and Land Grant Universities Council on Research Task Force on Laboratory Safety entitled "A Guide To Implementing A Safety Culture In Our Universities[53]," which provides recommendations and guidance on strategies to enhance the culture of laboratory safety and calls on institutions to commit to improving the culture of safety. A laboratory safety webinar based on the guidance document is also offered.

7. Compendium of Veterinary Standard Precautions[54]

The National Association of State Public Health Veterinarians developed this guidance to minimize transmission of zoonotic pathogens to veterinary personnel.

H. Conclusions

The US has a comprehensive framework for biosafety and biosecurity oversight. Extensive Federal regulations and guidelines exist to protect the safety and security of laboratory workers, the public, agriculture, and the environment. These Federal requirements are supplemented by numerous voluntary accreditation systems and standards that promote best practices to strengthen institutional biosafety and biosecurity programs. Institutions conducting life sciences research should have in place governance structures that ensure compliance with Federal biosafety and biosecurity requirements and guidelines. These structures may include a number of institutional oversight committees such as the IBC and the IRE. A number of institutional offices and departments are also responsible for the day to day activities that ensure compliance such as the conduct of inspections and training. Senior institutional officials also have responsibilities, not only for ensuring compliance in specific roles such as the Responsible Official at institutions subject to the SAR, but also for promoting and supporting biosafety and biosecurity broadly across their institutions.

Regulations or guidelines alone cannot ensure safe, secure, and responsible practices in the laboratory. Building a culture of biosafety and biosecurity involves achieving a congruent set of behaviors, attitudes, and policies that enable a person or an organization to work in a safe and secure manner with biological agents and toxins, and having a process by which individuals and organizations respond appropriately and effectively to biological hazards. FESAP Recommendation 1.1[55] was to create and strengthen a culture that emphasizes biosafety,

[53] http://www.aplu.org/library/safety-culture/file
[54] http://www.nasphv.org/Documents/VeterinaryStandardPrecautions.pdf
[55] http://www.phe.gov/s3/Documents/fesap.pdf

laboratory biosecurity, and responsible conduct in the life sciences. This culture of responsibility should be characterized by individual and institutional compliance with biosafety and laboratory biosecurity regulations, guidelines, standards, policies and procedures, and enhanced by effective training in biorisk management. Additional guidance documents and tools related to promoting a culture of responsibility can be found at the links below[56,57]. Biosafety and biosecurity cultural competency will complement and reinforce the knowledge and skills acquired through biosafety and biosecurity training (including compliance with rules and regulations). Such competency depends on effective risk communication based on a desire to protect the health and safety of people and the environment while maintaining the public trust in the biomedical research enterprise.

While this document was developed to provide guiding principles and best practices for ensuring appropriate biosafety and biosecurity governance structures are in place at institutions, with the democratization of science today not all biological research is conducted in a traditional institutional setting. All those conducting research in the life sciences are encouraged to apply the principles and practices articulated in this document to promote good stewardship and responsible conduct of research.

[56] Mitigating Insider Threats through Strengthening Organizations' Culture of Biosafety, Biosecurity, and Responsible Conduct, available at http://sites.nationalacademies.org/cs/groups/dbassesite/documents/webpage/dbasse_177312.pdf

[57] Available on the ABSA Training Tools webpage (under "Misc Handouts/Posters") at https://absa.org/training/