

Fast Track Action Committee Report: Biosafety and Biosecurity

PRODUCT OF THE
Subcommittee on Biological Defense
Research and Development
Committee on Homeland and National Security
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About the Fast Track Action Committee on Biosafety and Biosecurity

Since August 2014, the Administration has conducted a comprehensive review of the Federal Government's biosafety and biosecurity enterprise. One component of that review was creation of a Fast Track Action Committee on Select Agent Regulations (FTAC-SAR), which engaged broadly with external stakeholders to review the current regulatory controls over biological select agents and toxins and recommend improvements. The FTAC-SAR's report, issued in October 2015, contained a number of issues for further study. This FTAC – the Fast Track Action Committee on Biosafety and Biosecurity (FTAC-BIO) – was chartered to follow up on two of them: consider whether, and if so how, to bring all U.S. bioscience institutions, or at least all those operating at or above Biosafety Level 3 or "high containment", under Federal biosafety regulation; and explore whether and how the Federal Government could adopt a "risk-based" approach to managing the safety and security oversight of biological agents and toxins that did not depend on designating specific agents and toxins.

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INTRODUCTION

Purpose and Scope of the Fast-Track Action Committee

In 2015, the Biological Defense Research and Development Subcommittee (BDRD) of the National Science and Technology Council's Committee on Homeland and National Security chartered a Fast-Track Action Committee on Select Agent Regulations (FTAC-SAR) to solicit input from a wide range of stakeholders regarding how the Select Agent Regulations (SAR) have impacted science, technology, and national security in the United States. The FTAC-SAR's report describes findings and makes recommendations to improve the regulatory process and address perceived gaps in the SAR.¹

The FTAC-SAR report also identified more complex issues that required additional analysis before specific proposals could be developed and evaluated. FTAC-SAR recommended continued analysis of these issues to determine whether concrete approaches could be developed for addressing them. As a result, the BDRD chartered a new FTAC, the FTAC on biosafety and biosecurity (FTAC-Bio), to pursue further analysis of two issues in particular:

- **Institutional Scope of Biosafety Regulation:** Consider whether to bring all bioscience institutions in the United States that utilize potentially hazardous infectious agents under Federal biosafety oversight.
- **Risk-based Approach:** Explore the feasibility of adopting a “risk-based” approach to managing the safety and security oversight of biological agents and toxins.

In February 2016, FTAC-Bio initiated efforts to gather input from relevant stakeholders on these two related but distinct issues. The committee solicited input from academic administrators, government officials, professional societies, and other stakeholders. The committee combined this input with its own research and subject-matter expertise to formulate a set of ideas for consideration.

The background information provided in this section is designed to help set the stage for the deliberative options developed by the FTAC-Bio. Within the two overall objectives that have been identified above, this report considers four sets of issues: (1) Institutional Biosafety Committees; (2) Institutional Biosafety Program Accreditation; (3) the Occupational Safety and Health Administration (OSHA) Infectious Diseases Rulemaking Process; and (4) Risk-based Approaches to Biosafety and Biosecurity Oversight.

The scope of activities considered by the FTAC-Bio includes those in all sectors (government [Federal, State, and municipal], academia, privately funded research institutions, and private industry) utilizing disease-causing biological agents, or pathogens. The activities covered include work with human pathogens and zoonotic agents that can infect both animals and humans. Also included are related activities such as the maintenance of facilities and equipment, and administrative policies needed for effective biosafety, incident-reporting, and public outreach and communication efforts.

Brief Summary of the Evolution of Biosafety and Biocontainment Practices

Work with infectious agents in the laboratory always involves risk. Federal, State, and municipal

¹ National Science and Technology Council, Committee on Homeland and National Security, Subcommittee on Biological Defense Research and Development, Fast Track Action Committee on the Select Agents Regulations, “Recommendations on the Select Agent Regulations Based on Broad Stakeholder Engagement,” October 2015, (<https://www.phe.gov/s3/Documents/ftac-sar.pdf>)

entities, as well as scientists and individual research institutions, have taken numerous steps to mitigate those risks. As the Federal Experts Security Advisory Panel wrote in its December 2014 report.²

These risks are minimized by appropriate design, construction, and operation of the laboratories where this work is performed. However, the only way to completely eliminate these risks would be not to do the work at all, which presents a different set of risks – that diseases will not be detected or diagnosed, that treatments or mitigation measures will not be developed, or that disease outbreaks will not be controlled.

The development of biosafety and biocontainment practices and procedures has paralleled the development of the science of microbiology and its extension into new and related areas such as recombinant and synthetic nucleic acid molecule technology and human gene therapy.

Many of the biosafety/biocontainment practices and procedures in use today resulted from the efforts of U.S. scientists at Fort Detrick in the 1950s and 1960s.³ Since then, practices and policies have evolved, and protective equipment and containment systems have been developed. This evolution has led to the publishing and regular updating of today’s collection of Federal 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

The Federal Government has created multiple complementary and sometimes overlapping biosafety and biocontainment oversight mechanisms (Figure 1). Characteristics of biosafety and biocontainment oversight vary by facility and activity. Several oversight structures are described below.



² “Report of the Federal Experts Security Advisory Panel,” December 2014, <http://www.phe.gov/s3/Documents/fesap.pdf>

³ Reynolds M. Salerno, Jennifer Gaudio, *Laboratory Biorisk Management: Biosafety and Biosecurity* (CRC Press, Boca Raton: 2015), pp. 40-41.

- Regulatory
- Voluntary
- Condition of Funding

Notes: Graphic modeled on Figure 1 in “Report of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight,” July 2009, p. 41. <https://www.ars.usda.gov/is/br/bbotaskforce/biosafety-FINAL-REPORT-092009.pdf>. Shape areas do not necessarily represent the scope of research governed by a policy.

Figure 1. Overlap of Biosafety and Biocontainment Regulations, Standards, and Guidelines Pertinent to High and Maximum Containment Research

The Federal Select Agent Program (FSAP) promotes laboratory safety and security by enforcing the Select Agent Regulations (SAR), providing guidance to the regulated community, and inspecting facilities where work with select agents and toxins occurs. The FSAP originated from the Antiterrorism and Effective Death Penalty Act of 1996,⁴ due to heightened concern about the ease of obtaining disease-causing agents legally for illegal purposes. The 1996 legislation directed the Department of Health and Human Services (HHS) to establish a list of biological select agents and toxins (BSAT) with the potential to threaten public health and safety and to develop procedures governing the transfer of those agents. Legislation enacted after the 9/11 terrorist attacks and the anthrax letter mailings requires all individuals and institutions working with these biological agents to be registered with the U.S. government and mandates HHS and the Department of Agriculture (USDA) to establish by regulation a set of safety, security, and incident response procedures.⁵ This legislation affords the government an awareness of where BSAT work is conducted, who works with agents, and how agents are manipulated.

Institutional Biosafety Committees (IBCs) uphold biosafety standards in National Institutes of Health (NIH)-funded institutions that conduct recombinant and synthetic nucleic acid research. IBCs are responsible for determining necessary containment levels, evaluating facilities, assisting with Principal Investigator (PI) and laboratory staff training, ensuring that laboratory incidents, including exposures, are appropriately responded to and reported, and reviewing the portfolio of all research conducted at the institution to ensure compliance with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*.⁶ At present, the use of Institutional Biosafety Committees (IBCs) is only required for experimentation covered by the *NIH Guidelines*, which in turn are binding only for institutions that receive NIH funding. Other federal funding agencies may also require compliance with the *NIH Guidelines* as a term and condition of award. Beyond the review and oversight activities that are required under the *NIH Guidelines*, additional biosafety oversight responsibilities may be performed voluntarily at the institution’s discretion. These additional activities delegated to the IBCs are largely institution-specific and not standardized. In addition, the *NIH Guidelines* is a risk-based, performance driven document. Institutions have the latitude to develop their own policies and procedures to meet the biosafety oversight performance standards articulated by the document, based on institutional research risks. This gives research institutions the flexibility to structure their biosafety oversight programs in ways that best meet the needs of their very diverse research portfolios.

⁴ Public Law No: 104-132

⁵ Public Law No: 107-188

⁶ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, available at: <http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines>.

However, the lack of standardized IBC operating procedures may result in a lack of consistency in the rigor of biosafety oversight at institutions.

*Biosafety in Microbiological and Biomedical Laboratories (BMBL)*⁷ is guidance jointly published by the Centers for Disease Control and Prevention (CDC) and NIH that has become a code of practice for biosafety and biocontainment in U.S. microbiological and biomedical laboratories. The *BMBL* includes agent summary statements to describe a range of biological hazards, and it recommends precautions and levels of containment appropriate for handling specific human and zoonotic pathogens in laboratories and other facilities that house laboratory vertebrate animals. Specifically, the *BMBL* delineates four ascending levels of containment for work with biological agents that are hazardous to humans, referred to as biosafety levels (BSL) BSL-1, BSL-2, BSL-3 (high containment), and BSL-4 (maximum containment). Each level of containment adds to the previous level and 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*.

The Occupational Safety and Health Act requires all employers under OSHA jurisdiction⁸ to provide their employees with workplaces that are “free from recognized hazards that are causing or likely to cause death or serious physical harm.”⁹ Even in the absence of more specific regulation, this “General Duty Clause” requires employers to practice due diligence in protecting their workers from harm. More specifically related to biosafety, OSHA has issued a Bloodborne Pathogens Standard¹⁰ that states what covered employers must do to protect workers who are occupationally exposed to blood or other potentially infectious materials. This standard addresses, but is not restricted to, workers in clinical or research laboratories, with research laboratory workers constituting only a small fraction of those who are covered.

INSTITUTIONAL SCOPE OF BIOSAFETY REGULATION

The deliberative options identified below could supplement other current oversight mechanisms such as the SAR, *NIH Guidelines*, and the OSHA Bloodborne Pathogens Standards (29 CFR 1910.1030) at all bioscience institutions in the United States that use hazardous infectious agents.

Institutional Biosafety Committees (IBCs)

One challenge for improving biosafety procedures as they relate to IBCs is maintaining flexibility at the institutional level, where it is needed, while simultaneously sufficiently standardizing the system to promote consistent and effective biosafety practices throughout the country. Under the *NIH Guidelines*, which articulate the responsibilities of IBCs, it is a requirement for any institution subject to the *NIH Guidelines* to establish an IBC to oversee research with recombinant or synthetic nucleic acid molecules; however, the *NIH Guidelines* do not limit the purview of the IBCs to only these research areas. In practice, over four-fifths of IBCs registered with NIH have a broader biosafety oversight program

⁷ Biosafety in Microbiological and Biomedical Laboratories, available at: <https://auth.osp.od.nih.gov/external-resource/biosafety-microbiological-and-biomedical-laboratories-bmbl>.

⁸ Workers at state and local government agencies are not covered by Federal OSHA, but have OSH Act protections if they work in those states that have an OSHA-approved state program. The OSH Act does not cover the self-employed; immediate family members of farm employers; and workplace hazards regulated by another federal agency (for example, the Mine Safety and Health Administration, the Department of Energy, or the Coast Guard). https://www.osha.gov/Publications/all_about_OSHA.pdf.

⁹ Occupational Safety and Health Act of 1970 (29 USC 654, 5(a)1).

¹⁰ Title 29 CFR 1910.1030.

than what is specifically required under the *NIH Guidelines*.¹¹ IBCs are not required to follow standardized procedures in areas including scope, management, and frequency of training. Stakeholders consider the flexibility that the *NIH Guidelines* leave to institutions to determine practices that fit their specific needs as a strength.

Modifying the scope and extent of IBC activities could promote biosafety. Stakeholders have also encouraged IBCs to broaden their purview to include review of all high risk protocols (e.g., in the Fifth Edition of the *BMBL*).¹² Institutions, funders, professional organizations, and relevant government entities **should consider encouraging or requiring IBCs to cover more than recombinant and synthetic nucleic acid research**. This could be done in two non-exclusive ways. First, language encouraging the expansion of IBC oversight to include all work with infectious microorganisms and hazardous biological materials could be added by NIH and CDC to the *BMBL*. Such an action would convey the expectation that IBCs oversee institutional biosafety generally and not just biosafety activities for research involving recombinant or synthetic nucleic acid molecules. However, since adherence to the *BMBL* is voluntary, unless otherwise required by a funding agency—in contrast to the *NIH Guidelines*, which are a term and condition of award for recipients of federal NIH funding for research subject to their scope, this option would not necessarily improve the consistency of biosafety practices across the spectrum of relevant activities.¹³

A second option is for NIH to expand the scope of the *NIH Guidelines* such that their scope extends beyond recombinant and synthetic nucleic acid research, thereby requiring IBCs for recipients of federal funding to review projects and train personnel for a larger subset of microbiological research. Given the binding nature of the *NIH Guidelines*, this option holds promise for enhancing biosafety oversight broadly. However, expansion would concomitantly increase the regulatory burden the *Guidelines* impose, requiring that all labs, including those in private companies, that receive federal funds for research within the new scope, conduct IBC reviews, make IBC minutes available to the public upon request, and comply with the reporting and other requirements of the *NIH Guidelines*.

Both of these approaches would require an evaluation and significant rewriting of the *BMBL* or the *NIH Guidelines*. Both approaches would require careful consideration of issues such as whether additional requirements might impose additional financial and administrative burdens on institutions and impede the pursuit of scientific research.

Another approach to improving and encouraging consistency in IBC activities is to share best practices across biosafety programs at different institutions, which within the Select Agent community was one of the recommendations of the FTAC-SAR.¹⁴ Many institutions may have additional safety committees in addition to IBCs that are not mandated by the *NIH Guidelines* but are also designed to protect laboratory workers, the environment, and the public. Together, the IBC and other biosafety

¹¹ Raymond W. Hackney, Theodore A. Myatt, Kathleen M. Gilbert, Rebecca R. Caruso, and Susanne L. Simon. “Current Trends in Institutional Biosafety Committee Practices.” *ABSA: Applied Biosafety* 17.1 (2012): 11-18.

¹² See *Biosafety in Microbiological and Biomedical Laboratories*, p. 19, available at: <https://auth.osp.od.nih.gov/external-resource/biosafety-microbiological-and-biomedical-laboratories-bmbl>.

¹³ Adherence to the *NIH Guidelines* is a term and condition of award for recipients of NIH funding for research that is subject to their scope; NIH does not require adherence to the *BMBL*. At least one federal agency, DHS, does require adherence to the *BMBL* as a term and condition of award.

¹⁴ FTAC-SAR report, Recommendation 3: Sharing Best Practices: The FTAC recommends members of the regulated community establish a mechanism for sharing best practices.

review committees as well as the biosafety officer (BSO) and his/her staff are responsible for an institution's biosafety program. Most institutions' biosafety programs are coordinated through the biosafety office, with the BSO serving on the various institutional biosafety review bodies, including IBCs, relevant to that institution. An alternative approach to promote biosafety could be a mechanism involving oversight of institutional biosafety programs rather than expansion of IBCs. Any attempts to modify IBC scope, in the ways mentioned above or otherwise, should take into account the roles of non-IBC committees and biosafety offices in promoting biosafety within institutions.¹⁵

Accreditation of Institutional Biosafety/Biocontainment Programs

Accreditation can also demonstrate an institutional commitment to biosafety and biocontainment, demonstrate accountability and compliance with set standards, and provide an oversight system. Accreditation of an institutional biosafety program is the objective assessment of an institution's biosafety or biorisk management program by an independent body.

While the *NIH Guidelines* authorize NIH to withhold research funding from noncompliant institutions,¹⁶ they do not require IBCs or biosafety management programs to seek third-party assessment and accreditation to demonstrate that they are compliant with safety standards for overseeing recombinant or synthetic nucleic acid molecule research. Accreditation could be an effective mechanism to validate robust programs or guide improvement where needed. In addition, if the role of the IBCs were to be broadened (whether through incorporation in the *BMBL* or revision of the *NIH Guidelines*), **accreditation could be helpful in assuring risk mitigation measures properly address all research risks.**

Other institutional oversight boards, such as Institutional Review Boards (IRBs), which are required by law¹⁷ for research involving human subjects, regularly seek accreditation. All major U.S. independent Institutional Review Boards and 60% of U.S. research-intensive universities have applied for or attained accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP).¹⁸ Institutional Animal Care and Use Committees (IACUCs), which are required by law¹⁹ for research involving animals, have training requirements for participation on the committee and are part of the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation process. AAALAC has accredited animal research programs in over 950 companies, universities, hospitals, government agencies, and other research institutions worldwide that use animals.²⁰

AAHRPP and AAALAC accreditation processes have several features that could be applied to the accreditation of an institution's biosafety or biorisk management program. The AAHRPP assesses an institution's Human Research Protection program by conducting rigorous site visits and evaluating

¹⁵ The Federal Experts Security Advisory Panel (FESAP) 2.4 has bearing on this issue: "Modify guidance documents to recommend that the composition of the local oversight committee(s) represent the breadth of stakeholders involved in developing and implementing institutional biosafety and biocontainment programs."

¹⁶ As per *NIH Guidelines*, Section I-D: "As a condition for NIH funding of recombinant or synthetic nucleic acid molecule research, institutions shall ensure that such research conducted at or sponsored by the institution, irrespective of the source of funding, shall comply with the *NIH Guidelines*."

¹⁷ 42 USC § 289 (Institutional review boards; ethics guidance program); 45 CFR Part 46 (Protection of Human Subjects)

¹⁸ See <http://www.aahrpp.org/learn/considering-accreditation/value-of-accreditation>.

¹⁹ Title 7 USC § 2131 et seq. (Animal Welfare Act); 9 CFR § 2.31 (Institutional Animal Care and Use Committee).

²⁰ See <http://www.aaalac.org/about/index.cfm>.

the institution's IRB, program organization, and research staff. Within each of these three "domains of responsibility" are standards of procedure and expected outcomes to which the program must adhere in order to attain accreditation. AAHRPP publishes the names of accredited organizations and encourages those organizations to publicize their own accreditation. Accredited organizations renew their certifications three years after the initial accreditation and every five years thereafter. AAALAC follows a similar application and review procedure for laboratory animal research protection programs, but requires that organizations be visited every three years to maintain their accreditation status. These accreditation programs encourage institutions to comply with standards and incentivize institutions to promote compliance.

Accreditation of a biosafety program modeled on those outlined above could improve biosafety by promoting the establishment of a minimum set of biosafety standards, incentivizing biosafety programs to comply with them, and promoting a broader institutional interest and investment in biosafety. Furthermore, studies have reported that many IBCs are understaffed and underfunded by their institutions;²¹ accreditation could incentivize institutions to dedicate more resources to their IBCs and to their biosafety programs more generally.

Accreditation is an effective mechanism to identify and guide opportunities for improvement in standards implementation where needed. However, accreditation is costly to implement and would require expansion of the existing accreditation programs. Three approaches to accreditation are possible: formal third-party accreditation, self-accreditation, and a peer-review process. A formal third-party accreditation entity could provide a demonstration that biosafety programs adhere to a specified set of guidelines involving organizational roles and responsibilities in biosafety, IBC activities, and PI/researcher training. These criteria could be created by a consensus standards organization or by the individual IBC by drawing on existing language from an organization such as the American Biological Safety Association (ABSA International), or derived from defined biosafety guidance documents such as the *BMBL*. The International Organization for Standardization (ISO) is in the process of establishing a biorisk management standard (ISO/WD 35001), and it is anticipated to produce a final International Standard by 2019.²² Precursor documents already exist; the pending ISO standard draws from a previous effort, the European Committee for Standardization (CEN) Workshop Agreement 15793 (2011).²³ ABSA International runs a voluntary accreditation program, which includes biosafety and other performance measures; for BSL-2, ABSL-2, and BSL-3 laboratories; however, there are currently no third-party structures for accrediting IBCs. Requiring such accreditation is an option that needs further evaluation. NIH could promote accreditation by adding language to grant initiatives that encourages peer-review or the accreditation of biosafety programs funded by the institute.

A more easily implementable option is to establish a mechanism for institutions to self-accredit their institutional biosafety programs. A combination of assisted and self-accreditation may also be possible. In this scenario, institutions would conduct and provide documentation of self-accreditation based upon a predetermined set of guidance documents or the *BMBL*. Such efforts could be helpful in focusing institutional safety and security on areas that need improvement. It would be difficult, however, to confer preferential funding on institutions that self-accredit, given no independent way

²¹ Raymond W. Hackney, Theodore A. Myatt, Kathleen M. Gilbert, Rebecca R. Caruso, and Susanne L. Simon. "Current Trends in Institutional Biosafety Committee Practices." *ABSA: Applied Biosafety* 17.1 (2012): 11-18.

²² Personal communication, Dr. Jennifer Gaudioso, Sandia National Laboratories.

²³ European Committee for Standardization, "CEN Workshop Agreement (CWA) 15793, Laboratory Biorisk Management, 2011.

of comparing the rigor of assessments across institutions.

Institutions could also self-declare that their institutional biosafety programs meet specific standards and then assure their conformance by peer-review. A peer-review is conducted through a robust on-site review of all processes and standards to determine if the organization is indeed performing as declared. A peer-review can provide an independent way of comparing the rigor of assessments across institutions prior to a formal accreditation program.

Accreditation or peer-review should include, at a minimum, assessment of the institution's safety committee(s) that review bioscience work and biosafety training practices, and it should require that each institution keep records relevant to its work with infectious agents. Any consideration of these accreditation options should keep in mind the costs associated with obtaining accreditation, which might be particularly burdensome for smaller institutions to bear than larger ones.

OSHA Infectious Diseases Rulemaking Process

The FTAC-Bio was informed of OSHA's ongoing effort to create a standard to ensure that employers establish a comprehensive infection control program and control measures to protect employees from infectious disease exposures to pathogens that can cause significant disease. OSHA's Bloodborne Pathogens standard is currently in place (see Figure 1 for how these regulations overlap with other standards such as the *NIH Guidelines*); however, it does not address the risk of infectious agents transmitted by other means (e.g., contact, droplet, airborne). OSHA is currently developing an update to those standards; they cover employers engaged in providing healthcare and healthcare support services, handling contaminated materials, handling human remains, and operating biomedical laboratories (diagnostic, research, and production). It is anticipated that this OSHA regulation would establish a legally binding requirement to apply the biosafety concepts of guidance documents such as the *BMBL* and the *NIH Guidelines* to covered institutions, regardless of whether they receive U.S. government funding. As currently envisioned, however, it would not be prescriptive as to how those concepts should be implemented. The FTAC-Bio notes that the Federal Experts Security Advisory Panel (FESAP) has endorsed this OSHA Infectious Diseases standard in its most recent report, and the FTAC-Bio too supports the development of this standard in its currently proposed form.²⁴

Under the terms of the Occupational Safety and Health Act, OSHA regulations do not apply to workers at state and local government agencies, including public universities. States can establish State OSHA plans to cover state and local government workplaces, however, provided that State OSHA regulatory standards are "at least as effective" as Federal OSHA oversight of private sector employers. Currently 28 states or territories have OSHA-approved state programs that cover state and local government workplaces.²⁵ Public sector workers in states that have not established State OSAs would not be protected by this or any other OSHA regulation.

RISK-BASED APPROACH TO MANAGING SAFETY AND SECURITY

FTAC-SAR raised the issue of exploring the feasibility of a "risk-based" approach to biosafety and biosecurity regulation as a way to improve the flexibility and responsiveness of the current "list-based"

²⁴ Report of the Federal Experts Security Advisory Panel, December 2014: Recommendation 2.8 – "Support U.S. Occupational Safety and Health Administration (OSHA) Infectious Diseases Standard."

²⁵ See https://www.osha.gov/dcsp/osp/approved_state_plans.html.

SAR. Those regulations only cover agents and toxins that have been designated by the HHS and/or USDA Secretaries as select agents and toxins and that are so listed in the Code of Federal Regulations.²⁶

Risk-based management systems are common across many other industries, especially those in which accidents can have significant consequences.²⁷ Many high-consequence industries, including chemical, nuclear, petroleum, pharmaceutical, and airline, have abandoned generic, rule-based administrative systems in favor of more flexible risk-management systems. These industries have since achieved significant reductions in the number and severity of accidents. Recent security incidents at major bioscience facilities point to a need for increasing a culture of safety and security in the biological sciences.²⁸

The FTAC-SAR noted that multiple Federal and nongovernmental reviews and public comments collected in the past have expressed discomfort with basing the regulation of biosafety and biosecurity solely on whether the agents or toxins involved have been designated as select agents or toxins. Basing a regulatory regime on a list of agents provides a clear basis for the imposition of regulatory requirements; however, the FTAC-SAR has noted some limitations of such an approach, particularly from a security perspective:

- Pathogens that do not meet the criteria to be added to the select agent list may nevertheless pose risks to public health and safety. The magnitude of that risk depends on what manipulations or activities are being performed with or on them.
- Genetic manipulation of non-select agents may give them pathogenic or other properties equivalent to those of select agents, without their becoming subject to the SAR.

FTAC-SAR identified a need for analyzing whether a new regime could replace current safety and security requirements with a more risk-based approach that would be better able to address the full spectrum of biological risk, particularly those resulting from the evolution of biotechnology and research techniques.

In exploring this issue, FTAC-Bio notes—as did the FTAC-SAR—that the list of Select Agents and Toxins is based on risk. It was initially established on a risk basis; it is reviewed and potentially adjusted every two years, allowing for changes if risk assessments change, and it is currently divided into two tiers on the basis of risk, making it more accurate to call the Select Agent Regulations a risk-based, list-based system.

The system for overseeing biosafety that has been described in Section B of this report is also a risk-based system. Both the *BMBL* and the *NIH Guidelines* present approaches to assessing and mitigating risk that are commensurate with the level of risk associated with the pathogens involved and the manipulations being done to them. They are also able to accommodate newly discovered or created pathogens. However, what those guidelines lack and the SAR have is a legally enforceable scope. Unlike the SAR, these guidelines apply only to those institutions that voluntarily adopt them or that are recipients of government funding that requires them. Section B presented a discussion of various means by which their scope can be extended or how inconsistencies in their application might be

²⁶ Title 42 CFR §§ 73.3, 73.4; 9 CFR §§ 121.3, 121.4; 7 CFR § 331.3.

²⁷ Reynolds M. Salerno and Jennifer Gaudioso. *Laboratory Biorisk Management: Biosafety and Biosecurity*. 2015. Chapter 1: Introduction: The Case for Biorisk Management.

²⁸ *Ibid.*

resolved.

Security risks, on the other hand, are considerably harder to address with a flexible, risk-based approach than safety risks are. Some security controls—for example, access controls on dangerous pathogens—could in principle be applied on a near-real-time risk basis to novel, emerging, or engineered pathogens. However, other measures, such as conducting background checks on personnel with access to certain pathogens to guard against insider threats, must be done in advance. Unless everyone who might have access to any hazardous biological agents is subjected to advance vetting—a vast expansion of the current FSAP vetting that would have unacceptable consequences in terms of cost, civil liberties, and chilling necessary research—some criterion such as a list of Select Agents and Toxins will be necessary to determine who needs to be vetted.

Analysis and Conclusions. In the materials it reviewed and the briefings it received, FTAC-Bio did not encounter an approach that could preserve the basic security features of the current Select Agent Regulations without being based on a list of agents and toxins. But the FTAC-Bio’s mission was not to replace the current list-based system with a risk-based one, but rather to explore some of the consequences (both positive and negative) of a move in that direction. That task does not require a comprehensive analysis of the entire biosafety and biosecurity enterprise, but rather an understanding of the tradeoffs involved, some of which are not currently viewed as acceptable.

A list-based approach allows for unmatched clarity of roles and responsibilities in biosecurity between the institution and regulating bodies. The judgment of an institution is removed, and defined activities would be conducted by the Federal government or submitted for Federal level oversight (registrations, inspections, risk assessments of personnel, etc.). Moving along the spectrum from list-based toward risk-based necessarily shifts oversight to the local level, since Federal regulators could not be expected to make individual risk determinations that arise during a research institution’s day-to-day activities.

Rather than a list of pathogens with clear expectations, a risk-based approach would entail performance standards and general guidance for various research activities. Such an approach allows for more flexibility as risk evolves, and prevents one-size-fits-all solutions that can be challenging for the variety of institutions subject to policies and regulations. However, it would be poorly suited to incorporate those Federal actions and responsibilities that cannot be devolved to the institutional level, such as performing intelligence and law enforcement records investigations and background checks used to counter terrorism and other national security risks.

As discussed above, the size of the employee pool that would be subjected to pre-employment security vetting depends strongly on how sharply the requirements for such vetting can be defined. If vetting is only required for those having access to specified agents at known registered institutions, the pool can be limited. But if prior security vetting is deemed necessary for any scientist or engineer who might encounter or engineer a hazardous organism, the pool would become unacceptably larger.

In addition to the transition between centralization and decentralization, the shift from list-based to risk-based represents a shift from known and specified criteria to unknown and variable ones. As biotechnologies continue to evolve and be disseminated, their capabilities will continue to increase, and access to them will expand. This will certainly lead to greatly expanded beneficial applications, but the potential risks (both in terms of safety and security) will become more diversified and ever-harder for a list-based system to accommodate. A growing component of the biological “risk space” in the future will be posed not by those with physical access to select agents, but by those with the ability to manipulate or synthesize non-select agents in ways that give them equivalent potential for harm. As other risk reduction mechanisms (such as rapid medical countermeasure development) assume a greater role, the value of retaining traditional list-based select agent controls will need to be

reevaluated.

This report describes options that FTAC-Bio has considered that could strengthen oversight of biosafety in the United States. The options discussed in this paper—expanding the scope of IBCs, pursuing mandatory or voluntary accreditation or peer-review of biosafety/biocontainment programs, and this group’s full support for the current OSHA infectious diseases rule-making process—require consideration when thinking about improving biosafety and biosecurity in the United States.

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