NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

EVIDENCE-BASED LABORATORY BIORISK MANAGEMENT SCIENCE & TECHNOLOGY ROADMAP

A Report by the **Health Security Threats Subcommittee on Laboratory Biosafety and Biosecurity**

April 2022

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About this Document

To ensure biorisk management[1] is based on the best available science, the National Science and Technology Council's Subcommittee on Health Security Threats established the Applied

[1] Biorisk management includes an organization's coordinated and documented activities to prevent unintentional exposure within a facility (biosafety) or release of biological agents outside the facility (biocontainment) as well as to prevent theft, misuse, or intentional release of biological agents (laboratory biosecurity). Both laboratory biosecurity and biosafety are equally integral components of a comprehensive biological risk management system; the mitigations to reduce the risk of both are often complementary. The inextricable nature of safe and secure handling led the working group to adopt the collective term 'biorisk,' though not every aspect of biorisk is addressed by this working group.

Biosafety Research Working Group to identify and address research gaps needed to improve laboratory biorisk management, with the goal of ensuring that practices, guidance, and regulations are based on the best available science. The working group developed the *Evidence-based Laboratory Biorisk Management Science & Technology Roadmap*, which offers recommendations on how to advance applied biorisk research and employ the findings, as described in the Recommendations of this *Roadmap.* The Distributed Biorisk Research Landscape section of this *Roadmap* outlines the distributed stakeholder landscape for laboratory biorisk management, and the Applied Biorisk Research Priorities identifies priority biorisk management research areas based on initial engagements in federal and practitioner communities.

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Abbreviations and Acronyms

DOD Department of Defense

DOE Department of Energy

DOS Department of State

EPA Environmental Protection Agency

HHS Department of Health and Human Services

LAI Laboratory-acquired infection

NIST National Institute of Standards and Technology

NSTC National Science and Technology Council

OMB Office of Management and Budget

OSTP Office of Science and Technology Policy

R&D research and development

U.S. United States

USDA United States Department of Agriculture

USGS United States Geological Survey

Executive Summary

Sound laboratory biorisk management—which encompasses biosafety, biocontainment, and laboratory biosecurity—is essential for preventing and effectively responding to biological threats. Science-based biorisk management practices underpin the Nation's resilience against biological catastrophes, the vibrancy of the bioeconomy and biomanufacturing industries, and the public's confidence that work is carried out with the utmost attention to all aspects of biorisk management. Further, the devastating consequences of the COVID-19 pandemic demonstrated the catastrophic potential of biological threats on society and the importance of having an evidence-based scientific foundation to inform real-time biorisk management choices and to ensure state-of-the-art safe and secure practices.

The interagency Applied Biosafety Research Working Group was established in 2019 under the Subcommittee on Health Security Threats of the National Science and Technology Council's Committee on Homeland and National Security to identify and address research gaps needed to improve laboratory biorisk management, with the goal of ensuring that practices, guidance, and regulations are based on the best available science. For the purposes of this document, "biorisk research" refers to the systematic, scientific investigation into and study of materials, tools, facilities, practices, and management systems for the safe handling and containment of infectious microorganisms and hazardous biological substances. The working group developed the *Evidence-based Laboratory Biorisk Management Science & Technology Roadmap*. This *Roadmap* identifies biorisk management research topics, summarizes the challenges and opportunities of the distributed stakeholder landscape, and offers recommendations on how to advance applied biorisk research and employ the findings:

- Government-wide Coordination: Establish a community that coordinates and prioritizes applied biorisk research across Departments and Agencies in order to optimize federal resources needed to fill the applied biorisk research gaps.

- Biorisk Management Data-sharing: Develop mechanisms to share biorisk research results between Departments and Agencies, with international partners, and with the practitioner community to ensure relevant stakeholders have access to the scientific evidence.

- Globally Distributed Research Agenda: Encourage discussions towards sharing research priorities and discoveries on biorisk management practices with other nations, international organizations, and stakeholders to enable a sustainable approach to filling biorisk research gaps.

Introduction

"*United States international engagement to combat COVID-19 and advance global health security and biopreparedness is thus an urgent priority — to save lives, promote economic recovery, and develop resilience against future biological catastrophes*." – National Security Memorandum 1[2]

Background

Implementation of evidence-based laboratory management practices underpin the Nation's preparedness for biological threats, the vibrancy of the bioeconomy and biomanufacturing industries, and the public's confidence that work is carried out with the utmost attention to biosafety, biocontainment, and laboratory biosecurity. Biorisk management includes an organization's coordinated and documented activities to prevent unintentional exposure within a facility (biosafety) or release of biological agents outside the facility (biocontainment) as well as to prevent theft, misuse, or intentional release of biological agents (laboratory biosecurity). The COVID-19 pandemic demonstrated the urgency and impact of biological threats. Advancing evidence-based biorisk management is one key way to proactively mitigate biological incidents. For instance, the National Academies Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats, assembled at the request of the White House Office of Science and Technology Policy (OSTP), provided rapid expert consultations on several topics, including biorisk management and the effectiveness of various disinfectants and improvised, re-used, or less expensive personal protective equipment. Governments, the scientific community, and *ad hoc* groups worked commendably to quickly perform the needed research, but a pre-existing pipeline for applied biorisk research might have produced more rapid answers. The *Evidence-based Laboratory Biorisk Management Science & Technology Roadmap* outlines remaining biorisk research priorities to be answered and implemented in advance of the next biological incident.

Developing the scientific foundation for biorisk management practices supports U.S. priorities to advance global health security and develop improved preparedness against future biological threats. However, some laboratory biorisk management and related field[3] practices are based on antiquated research, risk aversion, or *ad hoc* protocols that lack a sufficient evidence base to support use of those practices (e.g., lack of quantitative data on various shower out procedures to reduce fomite transport). New knowledge gaps in science-based biorisk practices continually arise in diverse pipelines, like do-it-yourself (DIY) and engineering laboratories, diagnostic laboratories working with agents of unknown risks, and laboratories in low-resource settings where costs of maintaining a traditional biorisk management program may be prohibitive. The costs of not advancing the scientific foundation for laboratory biorisk management are manifold—such as increasing the risks of accidents, inadvertent exposures and releases by using ineffective or outdated practices in life science laboratories both at home and abroad or by failing to leverage science-based, cost-effective practices and facility design.

[2] National Security Memorandum 1: https://www.whitehouse.gov/briefing-room/statements-releases/2021/01/21/national-security-directive-united-states-global-leadership-to-strengthen-the-international-covid-19-response-and-to-advance-global-health-security-and-biological-preparedness/

[3] Many field practices include laboratory-related work and can be informed by laboratory biorisk research practices, such as biorisk practices surrounding specimen transport or diagnostic tests that occur outside of the laboratory.

Recognizing these issues, previous federal reports recommended the United States develop and maintain a robust program of applied biorisk research to create additional and update existing evidence-based practices and technologies.[4] Building the scientific foundation for biorisk practices is a consistent U.S. health security policy objective, most recently recognized in many of President Biden's priorities highlighting needed investments in biosafety, biocontainment, and laboratory biosecurity.[5] The OSTP research and development priorities and efforts related to securing the bioeconomy consistently emphasize the importance of evidence-based standards and practices. Properly assessing and enhancing the efficacy of biorisk practices will require a sustained and appropriately resourced research effort that keeps pace with rapid life sciences advancements and emerging biothreats.

[4] Report of the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight (2009, Objective 7 and Recommendation 7.1), Report of the Federal Experts Security Advisory Panel (2014, Recommendations FESAP 1.1, FESAP 1.6, FESAP 1.7), and Fast Track Action Committee Report: Recommendations on the Select Agent Regulations Based on Broad Stakeholder Engagement (2015).

[5] Examples: Multi-agency Research and Development Priorities for the FY2023 Budget (https://www.whitehouse.gov/wp-content/uploads/2021/07/M-21-32-Multi-Agency-Research-and-Development-Prioirties-for-FY-2023-Budget-.pdf) and American Pandemic Preparedness: Transforming our Capabilities (https://www.whitehouse.gov/wp-content/uploads/2021/09/American-Pandemic-Preparedness-Transforming-Our-Capabilities-Final-For-Web.pdf)

Recommendations

Building the Infrastructure to Sustainably Fill Science & Technology Gaps in Laboratory Biorisk Management

To achieve the vision of a sustainable approach to address research gaps in biorisk management, the Applied Biosafety Working Group has three overarching recommendations. These recommendations begin to set up the architectural framework for a biorisk research pipeline that is able to respond to today's and tomorrow's biorisk management challenges facing the life sciences across the One Health[6] spectrum. The communities developed through these recommendations can then identify, implement, and continually evaluate specific actions to build a strong scientific foundation for biorisk management.

Recommendation #1: Government-wide Coordination

Establish a federal community that coordinates and prioritizes applied biorisk research across Departments and Agencies to optimize federal resources needed to fill the applied biorisk research gaps.

- Rationale: Applied biorisk management transcends Departments' and Agencies' traditional mission spaces and requires coordination to both establish the scientific basis and employ those biosafety, biocontainment, and laboratory biosecurity practices based on the best available science.

- Function: This federal community could be launched as a voluntary technical working group and should consist of officials who have influence over applied biorisk research or related programs. This group should maintain awareness of the biorisk research landscape and carry out activities that leverage stakeholder communities to tackle the applied biorisk research priorities identified. This community should be the federal group that identifies where the United States is well-placed to interact with a globally distributed research agenda on biorisk management practices. This community could also address specific biorisk research gaps surrounding biosecurity, emerging or convergent technologies, and low-resource setting situations.

- Activities: This federal community should conduct coordination activities that optimally leverage federal expertise and resources. For example, this community could ensure federally funded research is not duplicative and apply lessons learned or best practices from individual Departments and Agencies across the Federal Government. This community should also identify and implement specific actions within the wider biorisk landscape that further biorisk research priorities. A specific action could be to incorporate biorisk components into existing extramural grant programs or to establish new programs that incentivize academic study of biorisk research priorities. Similarly, this community could engage researchers to include biorisk research knowledge gaps in pathogen-specific

[6] One Health is a collaborative, multisectoral, and trans-disciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes by recognizing the interconnection between people, animals, plants, and their shared environment.

scientific gap analyses. Furthermore, this federal community could coordinate and communicate U.S. priorities beyond the Federal Government and engage with the practitioner communities (life scientists, research safety professionals, or other stakeholders with an interest in biorisk management) to develop workable approaches for improving biorisk management.

Recommendation #2: Biorisk Management Data-sharing

Develop mechanisms to appropriately share biorisk research results and practices between Departments and Agencies, with international partners, and with the practitioner community to ensure relevant stakeholders have access to the scientific evidence.

- Rationale: Discoveries in biorisk management research should be directly and promptly applied to strengthen the global life sciences laboratories, bioeconomy, and biodefense enterprises, but mechanisms to disseminate biorisk research findings are limited. Avenues to share scientific findings in applied biorisk management range from institution-wide best practices and practitioner forums to publication in peer-reviewed journals, but these mechanisms can face roadblocks surrounding reputational or liability sensitivities.

- Function: Incentivize and encourage practitioners to disseminate evidence-based practices in biorisk management, possibly enabling new, effective channels for disseminating the information.

- Activities: The federal community in recommendation #1 could encourage practitioners to publish and share biorisk management research, both results and practices, that would benefit the life sciences community while minimizing potential security risks. This community could also support information sharing on best practices supported by evidence and identify barriers to efficient sharing between Departments and Agencies and international partners to balance access to data with data- and biosecurity challenges. Additionally, this community could support data-sharing on biorisk research not suited for traditional publication avenues, like real time problem-solving platforms between practitioners or narrow biorisk interventions, for immediate adoption.

Recommendation #3: Globally Distributed Research Agenda

Encourage discussions towards sharing research priorities and discoveries on biorisk management practices with other nations, international organizations, and stakeholders to enable a sustainable approach to filling biorisk research gaps.

- Rationale: World-wide, biorisk management guidance is becoming less prescriptive and more risk-based, and the global community has a shared interest in ensuring biorisk practices are based on the best available science. Multiple nations' support for applied biorisk research could amplify the benefits across the global scientific community and would optimize U.S. returns on investment for applied biorisk research. A research agenda distributed among multiple nations and stakeholders is a first step towards collectively fulfilling needed applied biorisk research.

- Function: Identify and assess current evidence gaps in laboratory biorisk management at all laboratory levels and develop an agenda for applied biorisk research. Such an agenda could provide the basis for future sharing of research findings across the global life science community, as appropriate and following federal laws and policies.

- Activities: In October 2020, the United States hosted the *G7 Experts' Meeting on Strengthening Laboratory Biorisk Management*,[7] during which the participants made the following recommendation:

  "*Recommend that the G7 sponsor one or more international workshops to identify and assess current evidence gaps in laboratory biorisk management at all laboratory levels and develop an agenda for applied biorisk research. The workshops should, where applicable, incorporate a "One Health" approach and include experts from both developed and developing countries. The research agenda should take into account ongoing related efforts in G7 and Global Partnership countries and other venues, including cooperative projects with developing countries. Such workshops could be incorporated into existing relevant forums or build from previous efforts, for example the International Experts Group of Biosafety and Biosecurity Regulators, Global Health Security Initiative Action Group, or World Health Organization's Consultative Meeting on High/Maximum Containment Laboratories, and be linked with the international technical working group also recommended by this G7 experts' meeting*."

[7] Meeting Report: G7 Experts' Meeting on Strengthening Laboratory Biorisk Management, Virtual, October 2020

The Distributed Biorisk Research Landscape

Building the scientific foundation for these applied biorisk research priorities transcends U.S. federal department mission spaces and resonates with international partners' interests and priorities. Many programs and communities are already aligned with evidence-based biorisk management and, if coordinated, further standardized, and amplified, could harness their respective communities to strengthen the scientific foundation for biorisk management. Therefore, an optimal approach to applied biorisk research is a distributed one—distributed between U.S. Government Departments and Agencies, stakeholders, and global partners. Such a coordinated and distributed approach will maximize return on investment for applied biorisk research, ensure relevance while minimizing duplication of effort and resources, and increase the dissemination and widespread application of evidence-based best practices in laboratories worldwide that face similar challenges.

A 2019 *Applied Biosafety Research Workshop* identified a number of stakeholders and opportunities to conduct applied biorisk research. These existing programs and communities provide the basis for coordination and collaboration and include federal biorisk research or pertinent programs, laboratory capacity programs, international laboratory networks, practitioner communities, knowledge institutions, as well as philanthropic organizations and cross-border organizations. Some examples of federal programs, as outlined in the Appendix, include:

- Centers for Disease Control and Prevention's Laboratory Safety Science and Innovation Intramural Research Fund Program
- Centers for Disease Control and Prevention's National Institute for Occupational Safety and Health (NIOSH) National Occupational Research Agenda (NORA) Program
- Department of Defense's Scientific Gaps in Biorisk Research Program
- National Institutes of Health's National Biosafety and Biocontainment Training Program
- Environmental Protection Agency's Homeland Security Research Program

As outlined above in Recommendation 1, government-wide coordination can optimize the use of federal resources that are needed to both fill the applied biorisk research gaps and coordinate with stakeholder communities. If brought together to tackle the challenge of sustainable biorisk management research, these stakeholders can achieve together more than any one of them could do on their own. For example, individual governmental Departments and Agencies could collaborate and coordinate their research priorities, compile their research findings, and optimize intra and extramural programs for the highest return on investment. International laboratory networks can leverage their individual expertise to tackle priority research, while laboratory capacity building programs can promote adoption of these evidence-based practices worldwide. The practitioner communities and non-governmental stakeholders can both identify key knowledge gaps and promote solutions. International organizations and international partners can also leverage their unique expertise and influence to collectively address challenges for the global community.

A 2020 *G7 Experts' Meeting on Strengthening Laboratory Biorisk Management* demonstrated that the importance of sound laboratory biorisk management is a shared priority. Experts in laboratory biorisk management from G7 countries discussed how evidence-based practices can be advanced and developed five recommendations for harnessing and amplifying ongoing work,

especially with respect to multilateral collaboration and scientific exchanges. These recommendations included:

- Sponsoring international experts' workshop(s) to develop a research agenda
- Beginning an ongoing international technical working group on evidence-based laboratory biorisk management
- Addressing projects within the research agenda via the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction
- Sponsorship of forums on evidence-based laboratory biorisk management
- Incorporating applied biorisk research topics in international research alliances

Finally, the Applied Biosafety Research Working Group concluded that a coordinated, distributed approach would also enhance resource efficiency for applied biorisk research projects. As very few federal agencies have dedicated funds for these projects, additional resources will be required to address the research priorities described in this *Roadmap* from within agency budgets. With effective coordination, as suggested in Recommendation 1, with a government-wide coordination group, a distributed approach would reduce expenditures by identifying collaboration opportunities to leverage resources and maximize impact.

Applied Biorisk Research Priorities

Prioritized and sustainably funded research to address biorisk knowledge gaps will further enable institutions to implement prospective, systematic, supported programs that enhance individual, institutional, and community biorisk management. To begin this multi-phased initiative, the 2019 *Applied Biosafety Research Workshop* engaged U.S. Government Departments and Agencies as well as biorisk experts and practitioners from outside the Federal Government, including professional societies, to identify knowledge gaps in biorisk management that would benefit from increased research. The workshop further sought to identify existing and potential opportunities within the federal landscape to fund and conduct applied biorisk research. The identified applied biorisk research priorities, while not the product of a literature review, derive from the workshop's findings and the working group members' expertise during deliberations.

For the purposes of this document, "biorisk research" refers to the systematic, scientific investigation into and study of materials, tools, facilities, practices, and management systems for the safe handling and containment of infectious microorganisms and hazardous biological substances. Importantly, these priorities included research related to decision making, management processes, and adherence to protocols. The inextricable nature of safe and secure handling led the working group to adopt the collective term 'biorisk,' though this document focuses specifically on the biorisk research gaps surrounding biocontainment that can be filled with scientific evidence and applied to laboratory-related work. These biorisk research findings will apply to the general handling of infectious materials, including waste management as well as laboratory and field response procedures, and include a distinct focus on human factors related to decision-making, review processes, and long-term (i.e., consistent and constant) adherence to safety protocols.

Evidence-based Evaluation of Elements within the Hierarchy of Controls

Evidence-based practices throughout the hierarchy of controls to reduce biorisk, including elimination, substitution, engineering, administrative controls, and personal protective equipment, protect the worker, the community, agriculture, and the environment. Several high-profile incidents at life science facilities have demonstrated the negative impacts that can occur when institutions conduct important basic and applied life science research within their core mission area without adequately addressing biorisk management issues. For example, inadequate inactivation protocols for high-risk agents could put workers, the public, and the environment at increased risk of exposure when these agents are transferred to or manipulated within a lower containment level laboratory.

Another area where a focused evidence base is critical is development of safe practices with new scientific equipment, tools, and methods. For example, the increased use of cell sorters for sorting unfixed cells in the 1990s and its associated risks led the International Society of Analytical Cytology to develop biosafety guidelines for sorting unfixed cells. These guidelines prompted cell sorter manufacturers to modify or design instruments specifically to prevent release of hazardous materials and work with their users to create a safe laboratory environment. As a result, most commercially available flow cytometers now have designs that reduce the formation of aerosols and have containment features that minimize the release of an aerosol outside of the sorting chamber.

Examples of Research Areas:

- Development and demonstration of validated pathogen inactivation, decontamination, destruction, and sterilization procedures
- Evidence-based protocols for laboratory and field techniques, including sample collection, transport or waste management, with scientific instruments and biotechnology tools, including various handling procedures and derivatization techniques
- Identification of risks and mitigation options for pathogen exposure associated with laboratory and field-based instruments, including modern and automated instruments
- Techniques to monitor contamination and validate disinfection, including real-time monitoring for automated systems, viability testing, bio-indicator tools, and context-dependent environmental sampling and stability
- Specifications for personal protective equipment for primary and secondary containment as well as optimal isolation practices post-exposure
- Specifications for decontamination methods, equipment, and facility controls

Scientific Basis to Prevent Pathogen Exposure and Infection

Recommended practices to minimize pathogen exposure and infection depend on the underlying scientific basis that informs a risk assessment or reliably leverages alternative approaches. Substitution with a less hazardous pathogen (or "surrogate") has long been a preferred method to reduce risk. Many experiments, including those focused on pathogen survival in the environment, aerosolization, transport, and transmission, can be conducted with a less pathogenic substitute or an inert particle and in a lower containment setting. However, to further the reliable use of these substitutions, scientific validation is needed. In a situation where substitution is not possible, a successful biorisk mitigation program relies on adequate knowledge of exposure pathways and hazard potential of the pathogen.

Examples of Research Areas:

- Characterization and handling of new or novel pathogens
- Validation of substitutions, including pathogen surrogates, that can be worked with safely and securely in lower containment settings
- Identification of reliable protocols, including standard procedures in various contexts and applications, to validate the use of substitutions or surrogates for hazardous pathogens
- Evidence to inform pathogen-specific biorisk assessment and management options (e.g., environmental survival, exposure routes, pathogenicity)
- Identification of metabolic, immunological, or other early indicators of exposure

Empirical Basis for Incidents: Human Factors and Equipment Reliability

To minimize laboratory-acquired infections (LAIs) and environmental releases, it is critical to understand the human factors and/or equipment failures responsible for such incidents. Informed biosafety decision-making and effective investment to minimize LAIs and environmental release depend on understanding the empirical basis for incidents. The traditional view of an incident is that it can be caused by human error (an accidental needle stick), equipment failure (a faulty air pressure sensor), or a combination of the two (panic after a leaked waste container). These are important factors that inform decision-making and review processes for planning work and enhancing workplace culture (see talent and workforce below).

Three types of data are critical to understanding causes of exposure incidents: root cause analysis of real-life incidents or near misses; general laboratory controls error analysis that can be applied to work with infectious materials; and workforce perception analysis of incidents. Often, each cause can be prevented with distinct biorisk management practices, but cost-effective interventions depend on understanding the science behind the relative risk.

Examples of Research Areas:

- Human Factors
    - Identification of the errors (e.g., fine or gross motor mishaps, protocol mistakes, violations, ignorance/lack of training, confusion, or working under stress) that drive laboratory-related incidents in a range of containment laboratory settings
    - Identification of the root causes for these errors, including the roles of human engineering, knowledge, mental state, or distractions
- Equipment and Controls Reliability
    - Identification of optimal specifications for life sciences equipment and instrument containment systems, including engineering controls, competency on equipment usage, and manufacturers' recommendations
    - Identification of biosafety engineering of equipment/instrumentation, including equipment placement and cross contamination, to minimize movement accidents in the lab
    - Identification of equipment fail-safe measures to ensure continuous function of research labs and prevention of the accumulation of hazardous materials

Evaluation of Risk Assessment Criteria and Biorisk Management Methods

The evolving life sciences landscape calls for updating biological risk assessment and management approaches, methods, and tools. The cornerstone of a successful biorisk management program is a robust and deliberate risk assessment to identify hazards and corresponding mitigation options. Unlike most chemical, physical, or radiologic hazards, the harm caused by biological hazards depends on complex interactions between the pathogen, host, and environment. Further, the outcomes of a biological incident can have secondary and tertiary consequences for the community/environment since biological agents can multiply and, in some cases, spread from host to host. The use of biological materials is expanding beyond traditional clinical or research laboratories into industrial and community-led environments, all while the tools to change the properties of a biological agent are becoming more widely accessible. In each of these nuanced contexts, achieving an acceptable level of risk requires evidence-based evaluations of various qualitative or quantitative approaches to risk assessment and management.

Examples of Research Areas:

- Identification of context-appropriate risk assessment methodologies (e.g., quantitative or qualitative), including those that apply outside the traditional laboratory (i.e., academic or federal) laboratory system (e.g., DIY practitioners)
- Cost-benefit analysis for engineering controls, biological engineering techniques, personal protective equipment, and biorisk mitigation/management programs across a variety of resourced settings to assess which equipment, processes, or procedures are most beneficial
- Evaluation of available risk and management assessment methods or tools in various life sciences work settings

- Identification of practical performance indicators to predict a successful biorisk management program

Talent and Workforce: Sociology of Laboratory Biorisk Management

Optimal biorisk mitigation depends on an enabling environment—personnel behavior, training, a management system, and organization culture—that should be informed with evidence from sociology, industrial and organizational psychology, and related fields. The goal to shift beyond compliance and into an environment where preventing incidents is the culture throughout an organization, as demonstrated by high reliability organizations such as the nuclear industry, is possible. Decision-making and review processes about biorisk management can influence both the likelihood of an incident occurring and the response to it. For example, sociological factors such as work tempo, preventative maintenance, and personnel stress may affect the examples of incidents in the "Empirical Basis for Incidents" above. Achieving this goal depends on key components, such as organizational leadership, biorisk management policy, management commitment, active engagement and training, and explicit roles or responsibilities, while also tailoring the components for the specific laboratory or context. But fundamental sociology research gaps remain and include identification of best practices, methods to implement a positive biorisk management culture, optimization of review processes, identification of factors that impede a culture of compliance in the workforce, and effective training methods for personnel. Building the sociological evidence base for biorisk management will enable effective and sustainable practices, procedures, and policies in a variety of settings where biosafety and biosecurity are needed.

Examples of Research Areas:

- Identification of evidence-supported practices for personnel management, including sociology and psychology studies surrounding workplace behaviors that support or impede a positive biosafety and biosecurity management culture
- Identification of factors in optimal design of biorisk management review processes (frequency of review, composition of reviewers, etc.)
- Identification of the appropriate resources that produce a successful biorisk management culture, including funds; administrative staff to reduce burden; incentivization and award programs; customized, frequent, career-long training; and routine proficiency evaluations
- Identification of the impediments and their solutions to building a proactive biorisk management culture, including reasons for non-compliance, metrics for a successful biorisk management program, and tailored techniques to improve biorisk management programs
- Description of effective approaches to biosafety training, biorisk communication, and transparency (for relevant staff, public, and stakeholders), including understanding the relationship between various approaches to biorisk teaching or managing in areas like accountability, workforce state of mind, or fear of reprisal and the number or severity of biological incidents

Appendix: Examples from the Distributed Biorisk Research Landscape

U.S. Government biorisk research and pertinent programs:

- Centers for Disease Control and Prevention (CDC) Laboratory Safety Science and Innovation (LaSSI) Intramural Research Fund Program: Funds projects that advance the science of safety and quality by generating new data or tools to inform best practices within the agency, across the country, and worldwide.
- CDC National Institute for Occupational Safety and Health (NIOSH) National Occupational Research Agenda (NORA) Program: Conducts occupational safety and health research, including research to assess whether infectious agents pose a hazard in laboratory and field settings.
- CDC Public Health Emergency Preparedness and Response Applied Research Program: Funds research, translation, and dissemination initiatives to strengthen and expand evidence-based practices that improve federal, state, local and territorial preparedness and response to all hazard emergencies.
- Department of Defense (DOD) Scientific Gaps in Biorisk Research Program: Funds DOD projects related to biorisk topics with Biological Select Agents and Toxins.
- National Institutes of Health National Biosafety and Biocontainment Training Program: Funds fellowships for applied occupational safety and health research.
- Environmental Protection Agency Homeland Security Research Program: Conducts research on public health pathogens in support of antimicrobial product registration and to effectively respond to and recover from natural or manmade disasters, including acts of terrorism that involve chemical, biological, or radiological weapons.
- Environmental Protection Agency Environmental Science Center: Houses more than 75 laboratories dedicated to organic and inorganic chemistry, biology, microbiology and other scientific activities.
- Department of Agriculture Research Alliance for Veterinary Science and Biodefense BSL-3 Network (RAV3N): Coordinates a network of 15 federal and U.S. academic institutions with a focus on animal health and biodefense, including an Operations/ Biosafety/Biorisk Working Group.
- Department of Homeland Security Science and Technology Directorate (DHS S&T) Probabilistic Analysis of National Threats Hazards and Risks (PANTHR) Program sponsors research at the National Biodefense Analysis and Countermeasures Center (NBACC): Characterizes biological threat agents to support national risk assessments, policies, and plans to prepare for and respond to natural or manmade crises involving chemical, biological, radiological, and nuclear materials.

U.S. Government capacity building programs

- CDC Center for Global Health and WHO Collaborating Center for Biosafety and Biosecurity: Aids in the development of international recommendations and guidance for laboratory biosafety and biological risk management.
- DOD/Defense Threat Reduction Agency (DTRA) Biological Threat Reduction Program: Funds laboratory capacity building projects to reduce the threat of deliberate, accidental, and natural infectious disease outbreaks resulting from especially dangerous pathogens by collaborating with partner countries to enhance biosecurity, biosafety, and biosurveillance measures.

- Department of State Biosecurity Engagement Program: Funds projects to increase biosafety and biosecurity awareness and best practices within a country or region through direct engagement with scientists, public and veterinary health workers, and government officials.

International laboratory networks

- Biosafety Level 4 Zoonotic Laboratory Network: Network of biosafety level 4 zoonotic laboratories in Australia, Canada, Germany, United Kingdom, and the United States that focuses on knowledge sharing and institutional cooperation, international response, scientific excellence, and training world-class personnel.
- Group of High Containment Laboratory Directors: Network of animal facility directors in Australia, Canada, China, Germany, Netherlands, United, Kingdom, and the United States that facilitates the sharing of best practices for biological risk management, training, and safe laboratory practices.
- Global African Swine Fever Research Alliance: Network of laboratories to sustain global research projects to prevent, control, and, where feasible, eradicate African swine fever.
- Global Foot-and-Mouth Disease Research Alliance: Network of laboratories to sustain global research projects to prevent, control, and, where feasible, eradicate foot-and-mouth disease.
- World Health Organization's Emerging and Dangerous Pathogens Laboratory Network: Network of high security human and veterinary diagnostic laboratories that assists WHO to enhance readiness and response for timely laboratory detection and management of outbreaks and to facilitate the transfer of safe and appropriate diagnostic technologies, practices, and training.

Practitioner communities, knowledge institutions, and cross-border organizations

- Professional Societies and Scientific Organizations: Numerous civil society and industry organizations as well as philanthropic organizations have a role in strengthening laboratory biorisk management, including the American Biological Safety Association-International, the International Federation of Biosafety Associations, and the Association of Public Health Laboratories.
- International Working Group on Strengthening the Culture of Biosafety, Biosecurity, and Responsible Conduct in the Life Sciences: An international working group of experts from governments and civil society that develops and disseminates educational materials to promote the culture of responsibility.
- The Global Partnership Biological Security Working Group: An international working group focused on coordinating programs on biological security threats, within the G7-led 31 member international initiative aimed at preventing the proliferation of biological, radiological, and nuclear weapons materials.
- International Experts Group of Biosafety and Biosecurity Regulators: An international working group of biosafety and/or biosecurity regulatory authorities from 11 member countries that have strong regulatory oversight in place for biosafety and biosecurity.
- International Veterinary Biosafety Working Group: An international workgroup of laboratory directors, biosafety advisors, and biocontainment engineers that works to promote best practice in microbiological biocontainment and safety in biosafety level 3 and 4 veterinary laboratories.

- The Global Health Security Agenda: Action Package Prevent-3 on Biosafety and Biosecurity: A partnership of nations, international organizations, and non-governmental stakeholders that promotes full compliance and tracks progress with biosafety and biosecurity targets as well as acts as a liaison between donors and recipients for effective capacity building.
- International Governmental Organizations: Numerous international organizations have a role in strengthening laboratory biorisk management, including the World Health Organization, the Biological Weapons Convention, the World Organization for Animal Health, and the Organization for Economic Co-operation and Development.