Global Biorisk Research Agenda

Strengthening Laboratory Safety through Development of a Research Agenda for Science-Based Biorisk Management

March 2026

Biorisk Research Agenda

This Page Intentionally Left Blank

This document, created by Deloitte Consulting, LLP,[*] was funded by a grant from the United States Department of State. The opinions, findings and conclusions stated herein are those of the authors and do not necessarily reflect those of the United States Department of State.

[*]Deloitte refers to one or more of Deloitte Touche Tohmatsu Limited, a UK private company limited by guarantee ("DTTL"), its network of member firms, and their related entities. DTTL and each of its member firms are legally separate and independent entities. DTTL (also referred to as "Deloitte Global") does not provide services to clients. In the United States, Deloitte refers to one or more of the US member firms of DTTL, their related entities that operate using the "Deloitte" name in the United States and their respective affiliates. Certain services may not be available to attest clients under the rules and regulations of public accounting. Please see www.deloitte.com/about to learn more about our global network of member firms.

Acknowledgements

We extend our sincere gratitude to the Planning Committee members for their pivotal role in shaping this Agenda. We also thank all contributing experts for their active engagement and insightful input in articulating community needs and priorities. Your collective efforts have laid a strong foundation for future research in biorisk management.

Acronyms and Abbreviations

ABSL	Animal Biosafety Level
ACH	Air Changes per Hour
ACL	Arthropod Containment Level
AGB	Above-Ground Burial
ASTM	American Society for Testing and Materials
BBP	Bloodborne Pathogens
BIBO	Bag-In Bag-Out
BIs	Biological Indicators
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BSC	Biological Safety Cabinet
BSL	Biosafety Level
CBEP	Cooperative Biological Engagement Program
CDC	Centers for Disease Control and Prevention
CFD	Computational Fluid Dynamics
CL	Containment Level
EPA	Environmental Protection Agency
HEPA	High Efficiency Particulate Air
HVAC	Heating, Ventilating, and Air Conditioning
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IBC	Institutional Biosafety Committee
ISO	International Organization for Standardization
KI-DISCUS	Potassium Iodide – Direct Inoculation of Spore Strips
LAI	Laboratory Acquired Infection
LBM	Laboratory Biosafety Manual
NIH	National Institutes of Health
NSF	National Sanitation Foundation
OCSPP	Office of Chemical Safety and Pollution Prevention
OSHA	Occupational Safety and Health Administration
PAPR	Powered Air Purifying Respirator
PC	Physical Containment
PPE	Personal Protective Equipment
r(s)NA	Recombinant or Synthetic Nucleic Acids
RODAC	Replicate Organism Detection and Counting
SOP	Standard Operating Procedure
ULPA	Ultra-Low Particulate Air
UN	United Nations
UN ECOSOC	United Nations Economic and Social Council
UV	Ultraviolet
WHO	World Health Organization
WOAH	World Organization for Animal Health

Table of Contents

Executive Summary

The Case for Safer Science

The rapid growth of life sciences research has improved global health but has also increased the need for robust protocols to prevent laboratory incidents. Yet, a significant gap remains in our understanding of how to best mitigate biological risks due to the lack of data supporting biosafety practices. This project, funded by the U.S. Department of State and implemented by Deloitte Consulting, provides the foundation for future work to strengthen and evolve biorisk management, underpinning scientific progress with safety and security measures that protect people, animals, and the environment.

Outdated Approaches, Uncertain Outcomes

Biorisk management encompasses the practices and policies used to identify, assess, and control risks associated with handling biological agents. Despite their critical role in safeguarding public health, contemporary biorisk management practices often rely on outdated or nonexistent research, anecdotal evidence, and unproven best practices. This lack of a strong empirical foundation creates uncertainty about the effectiveness of safety measures, hinders efficient resource allocation, complicates oversight, and places a greater burden on biosafety professionals and researchers.

Launched in response to a 2020 G7 recommendation, this Global Biorisk Research Agenda aims to catalyze research efforts that will modernize and strengthen laboratory biosafety practices, making them more effective at preventing incidents and protecting researchers, the community, and the environment. Evidence-based protocols not only make laboratories safer, but also build confidence among researchers, institutions, and the public while bolstering the credibility of the biosafety workforce. The Biorisk Research Agenda describes critical data needs recognized by the global biorisk management community, highlighting opportunities to strengthen current practices and proposing notional experimental designs for future research.

***Biorisk Management Research Priorities**. Experts identified more than 100 critical data needs across existing biosafety practices, containment infrastructure, and biorisk management systems and personnel.*

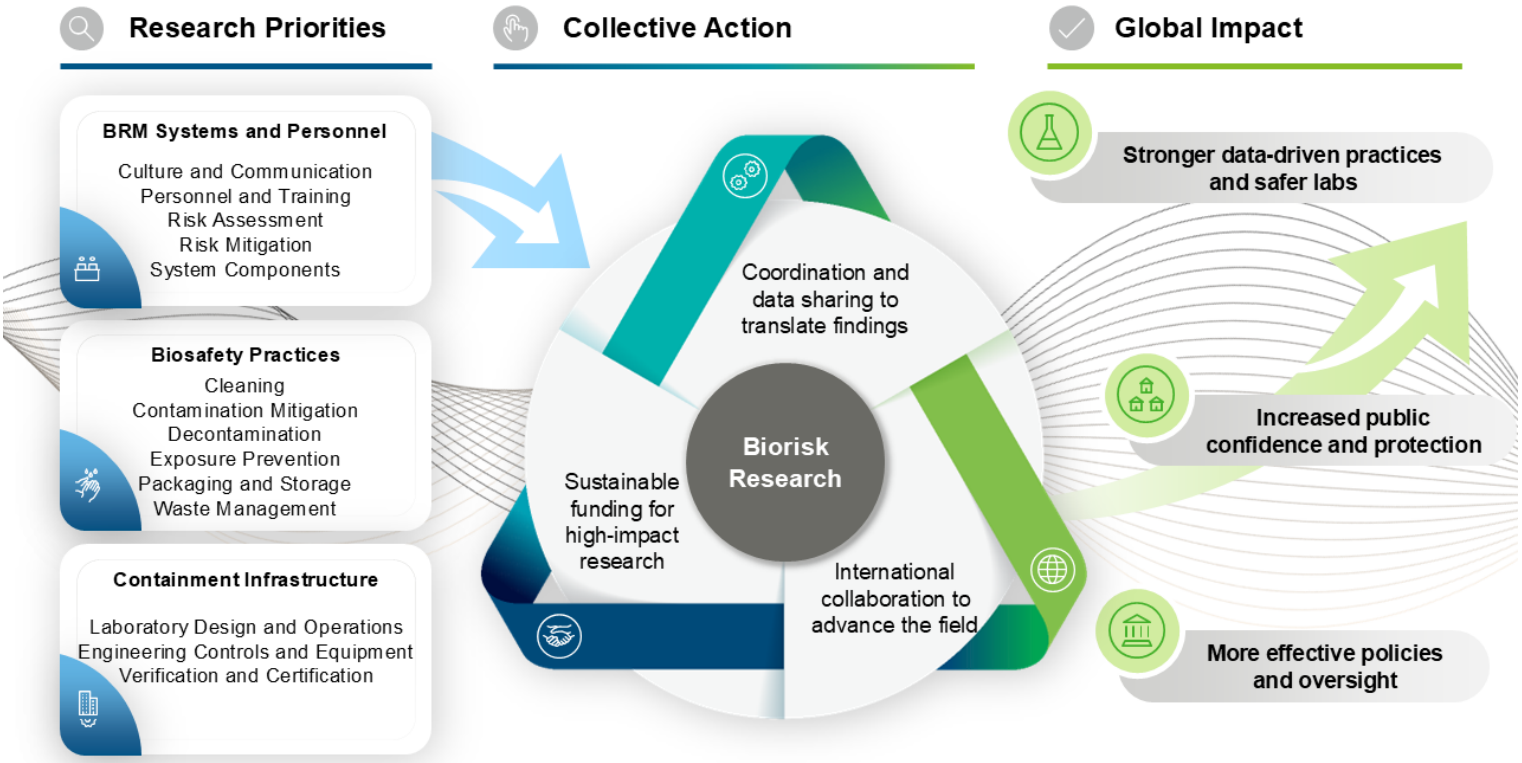
Progress through Global Collaboration

- Six international workshops brought together over 120 technical experts from more than 50 countries, recognizing that laboratory safety is a universal concern requiring global expertise.
- Experts identified more than 100 evidence needs spanning existing biosafety practices, containment infrastructure, and biorisk management systems and personnel.
- These insights shaped the Biorisk Research Agenda, which highlights opportunities to strengthen current practices and proposes notional experimental designs for future research across the life, physical, and social sciences.

Collective Action to Strengthen Laboratory Safety

- *Implement the Biorisk Research Agenda* to help laboratories make better data-driven decisions, improve how institutions manage safety, and provide stronger evidence for policies and oversight.
- *Secure sustainable funding* to enable high-impact research and lasting progress.
- *Establish mechanisms for coordination and reliable data-sharing* to ensure that findings are widely accessible and effectively translated into practice.
- *Foster the community* of professionals dedicated to evidence-based biosafety and strengthen international collaborations to advance the field.

As the life sciences continue to advance, biorisk management must also evolve to keep pace. By prioritizing evidence-based approaches and global collaboration, the Biorisk Research Agenda and subsequent efforts will empower laboratories worldwide to make informed, risk-based decisions, regardless of location or specialization.



Implementing the Global Biorisk Research Agenda*. Collective action by the global biorisk community can transform research priorities into evidence-driven practices, enabling lasting progress in laboratory safety.*

Introduction

The U.S. Government funded a project to identify high priority areas of applied biosafety research to improve laboratory biosafety, minimize laboratory incidents, and protect laboratory workers and the public.

To achieve this goal, this initiative was designed with several key objectives:

- Identify critical evidence needs within biorisk management to serve as the foundation of the Global Biorisk Research Agenda;
- Develop a framework for applied biosafety research opportunities to guide new efforts with the field; and
- Create a global network of stakeholders committed to improving biosafety practices and fostering ongoing collaboration.

Completion of the research studies included in the Biorisk Research Agenda will have significant implications for laboratories and stakeholders around the globe. Pathogenic biological agents do not recognize borders, so inadequate biosafety practices in a single laboratory can have far-reaching effects on global health security. Implementing evidence-based practices will benefit the safety of all types of laboratories at various resource levels, ranging from cutting-edge research facilities to diagnostic laboratories handling unknown organisms.

History of Biorisk Management

Biological research and laboratory medicine deliver profound benefits to societies worldwide—advancing human and animal health, driving discovery, and improving lives. Yet, this innovation is accompanied by inherent risks, particularly in laboratories handling high-consequence pathogens. Effective biorisk management—including biosafety and biosecurity measures for the handling, storage, and disposal of biological materials—is essential to prevent and mitigate these risks, including those posed by laboratory accidents. Biorisk management measures must be informed by scientific data to ensure that they truly protect people, animals, and the environment, yet many are not.

During the explosion of biomedical research in the 1950s, the field of biosafety began evolving from the more reactive, hygiene-oriented laboratory safety practices used up to that point into the modern practice that we recognize as biosafety today.[1] As research advanced, so too did the practice of biosafety and the discipline was broadly adopted during the smallpox eradication efforts of the 1960s and 1970s.[2] During this time, experts advocated for an approach that addressed the safety of a laboratory system based on an assessment of the risk associated with the biological agents in use and the procedures conducted with them in a specific laboratory space (i.e., a site-specific risk assessment).[2-4] Use of site-specific risk assessment for identifying and mitigating risks associated with the use of biological agents in specific laboratories is an effective means for tailoring risk mitigations to the local context; however, it can also be a time-consuming process that requires specialized expertise.

When the *Laboratory Biosafety Manual (LBM)* and *Biosafety in Microbiological and Biomedical Laboratories (BMBL)* were first published by the U.S. CDC in the 1980s, biorisk management moved toward the application of predetermined mitigation measures based on the biological agents used in the laboratory and the types of work being conducted (i.e., biosafety containment levels).[2,5,6] In contrast to the site-specific risk management model, biosafety containment levels use more of a "one size fits all approach" for implementation of standardized practices, equipment, and facility specifications. However, strict reliance on containment levels can be suboptimal due to a lack of consideration for particular research activities, local conditions, and insufficient evidence. Additionally, the significant increases in engineering control requirements between containment levels may result in the application of inappropriate or excessive controls that are not tailored to specific risks.[7,8] Containment levels can be used as a tool to support and streamline risk assessments for practitioners.

Gaps in Current Biorisk Management Practices

The current practice of biorisk management utilizes a hybrid approach that combines standards and predefined measures with site-specific risk assessments to tailor mitigation strategies to an individual facility and its specific activities. However, performing these risk assessments can be challenging for biosafety professionals because they must rely on limited and outdated research, anecdotal information, and unvalidated best practices. Efforts to validate commonplace practices or update data are hindered by limited funding, lack of research incentives, and an already overextended professional community. Beyond the scarcity of empirical data on biosafety measures, there is also a stunning lack of understanding of laboratory accidents or broader operational risks.[8,9] Furthermore, the evidentiary data that does exist is often published in academic journals that can be inaccessible to the biorisk management community due to paywalls, further restricting critical information needed to inform best practices.

In recent years, more high- and maximum-containment laboratories (e.g., BSL-3 and BSL-4, respectively)—those working with the most dangerous biological agents—have come on line around the world, and the creation of new scientific tools has led to vast expansion in the ability of scientists to create and modify microbial organisms.[8,10] As novel technologies continue to advance at unprecedented rates, as costs decrease to make research more accessible, and as new pathogens emerge, the gap between existing practices and the underlying evidence will continue to widen. Thus, there is a critical need to ensure that biosafety practices are based on the best available scientific evidence and are rigorously validated. This will safeguard people and communities while ensuring that these measures are implemented in the most efficient and least burdensome manner possible for the research enterprise.

To implement the G7 Expert's Meeting vision, on behalf of the U.S. Department of State's Bureau of Arms Control and Nonproliferation Office of the Nonproliferation and Disarmament Fund, Deloitte Consulting, LLP** has collaborated with global experts representing laboratories of all types and resource levels to develop this Global Biorisk Research Agenda. This initiative marks a pivotal step toward conducting the research needed to advance evidence-based biorisk management worldwide.

Development of the Global Biorisk Research Agenda

The Biorisk Research Agenda describes critical data needs recognized by the global biorisk management community, highlighting opportunities to strengthen current practices and proposing notional experimental designs for future research. Although not exhaustive, this agenda represents a shared set of priorities identified by the scientific community, intended to both drive high-impact research and underscore the wide range of work that is needed to ensure biosafety practices are firmly rooted in science. The international collaboration that shaped this Research Agenda has fostered a dynamic network of researchers and biorisk practitioners ready to contribute their expertise to advance the field and committed to the adoption of evidence-based practice.

Evidence-based practice will give scientists a clearer understanding of risks to themselves, their colleagues, the community, and the environment. Biorisk managers will be empowered to do their jobs more effectively, while institutions will be better equipped to allocate resources appropriately and ensure safe operations. Policy makers and regulators will gain a stronger foundation for oversight and the development of science-driven guidance and regulations. Ultimately, an evidence-based approach will not only strengthen research safety worldwide but also promote open communication, increase transparency, and build trust within the life sciences community and with the public.

The following aims will be addressed through the implementation of the Biorisk Research Agenda:

At the laboratory level:

- Verify that safety measures reduce risks to an acceptable and appropriate level, protecting personnel, public health, and the environment, without being overly stringent;
- Provide an evidence base for various approaches to mitigate risk, allowing practitioners to select resource-efficient, locally appropriate, and sustainable practices;
- Enable safety professionals to make data-driven recommendations, increasing buy-in from researchers and management for biosafety practices.

At the institutional level:

- Guide strategic allocation of necessary resources and support for biorisk management;
- Facilitate effective evaluation of biorisk management system health, enabling more informed decision-making and continuous improvement;
- Strengthen institutional governance and ability to demonstrate that activities comply with established local, national, and/or international standards and best practices.

At the oversight level:

- Provide quantitative assessments of risk to inform policymakers and regulators of the appropriate level of controls for biological facilities;
- Inform effective policies and standards grounded in real-world evidence, driving meaningful safety improvements and broader acceptance;
- Facilitate global harmonization by using evidence-based approaches to align safety standards and requirements internationally.

Globally Collaborative Development of the Biorisk Research Agenda

Biosafety is fundamentally a global issue, as laboratories across the world—regardless of location, size, or available resources—face similar challenges in ensuring the safe handling of biological materials. Moreover, an incident in any one laboratory could jeopardize public health and undermine nonproliferation efforts worldwide. With this understanding, the project team recognized that developing a comprehensive Biorisk Research Agenda would necessitate a globally collaborative effort. Only through such an approach could the agenda genuinely reflect the needs of laboratories worldwide and move toward addressing the varied challenges encountered across all types of work and resource settings.

An advisory committee was established to ensure this initiative was guided by broad expertise and perspectives. This committee consists of five seasoned biosafety and life science professionals representing a range of geographical regions and various international academic, governmental, non-governmental, and industry organizations. Members were intentionally selected for their deep and diverse expertise in biorisk management, biocontainment, and laboratory research, as well as their familiarity with both global and regionally topical issues. Throughout this project, the advisory committee provided critical guidance that shaped the development of the Research Agenda and aided its relevance and reach to scientific communities worldwide. The committee members, who participated in their personal capacities are:

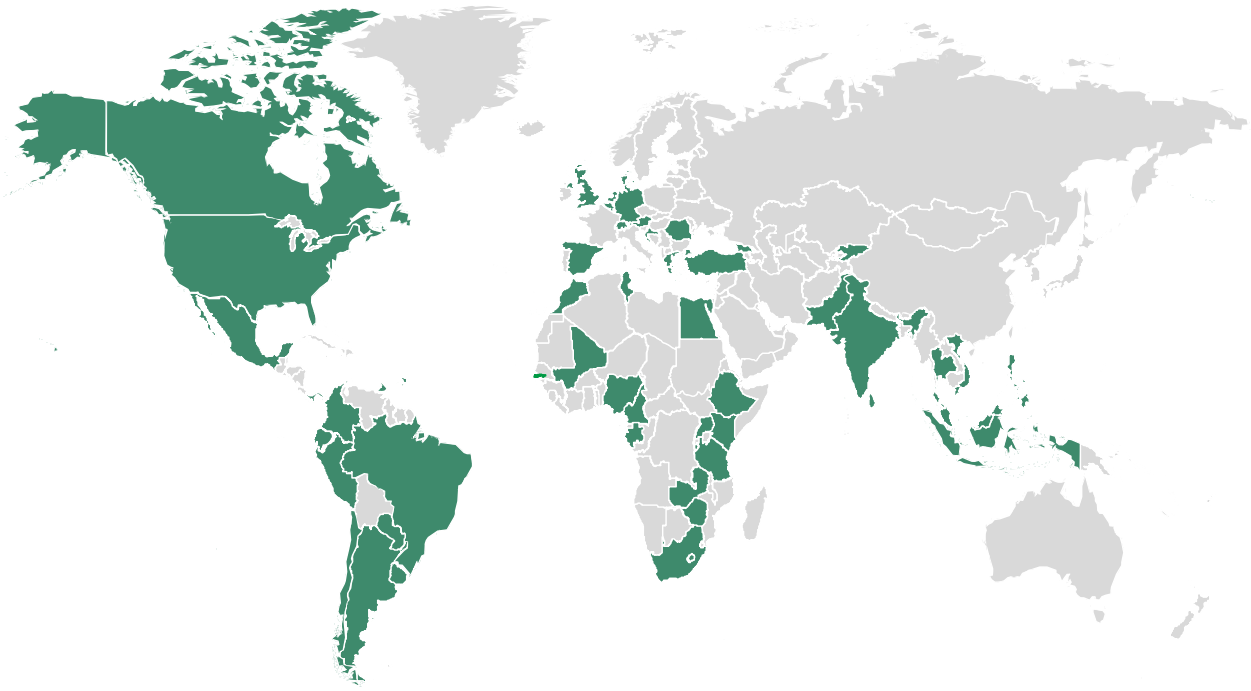
- Prof. Rakesh Bhatnagar, PhD (India)
- Kazunobu Kojima, PhD (Switzerland)
- Zibusiso Masuku, B.Eng (South Africa)
- Rebecca Moritz, MS, CBSP (U.S.)
- Lia Vizzotti, MSc, MBA, RBP (Colombia)

Launched in late 2022, the project began with a comprehensive review of scientific and grey literature Ito understand the current landscape of evidence-based biosafety practices and data needs already identified within the field. The team also conducted informal scoping discussions with multisectoral scientific and biorisk management experts that provided insights into the current priorities and perspectives of the biosafety community as well as firsthand input on shaping the project to ensure its outputs would be valuable and relevant to all stakeholders.

The development of the Biorisk Research Agenda was primarily driven by input from the global scientific community, gathered through a series of collaborative workshops held from February 2023 through December 2024. Workshops were strategically designed to allow for in-depth exploration of specific topics while also covering the full breadth of biorisk management. Over the course of the project, six workshops were convened alongside international scientific conferences in Argentina, Belgium, France, the Philippines, South Africa, and the U.S.

These workshops engaged more than 120 technical experts from more than 50 countries across all geographic regions, including biosafety officers, facility managers, containment engineers,

laboratory technologists, medical scientists, life science and clinical researchers, technical advisors, and policymakers from academia, industry, and government. Participants were selected based on their expertise and relevance to the workshop topics, ensuring varied and meaningful contributions. Each highly collaborative two-day workshop featured small group exercises and full group discussions designed to identify and map evidence gaps underlying biosafety practices, ideate on experimental protocols to address these gaps, and explore other barriers to advancing evidence-based biorisk management. Following each workshop, the project team synthesized the outputs, ensuring that all data needs and initial study designs developed by the subject matter experts were appropriately characterized, contextualized, and supplemented with additional details as needed in a summary report. Workshop contributors were subsequently invited to review and provide feedback on these reports.



Global Representation of Contributing Technical Experts. *Shaded countries indicate those represented by technical experts who contributed to the project; the number of experts per country may vary, with multiple attendees possible from the same country.*

Key Themes from the Research Agenda Workshops

Over the course of six collaborative workshops, members of the global biorisk management community identified practices and elements that lack sufficient evidence to reliably establish optimal safety measures. Together, experts designed experiments that span the life, physical, and social sciences aimed at generating the data necessary to inform and strengthen these practices. More than 100 of these critical data needs have been catalogued in the Biorisk Research Agenda, providing a framework to guide future applied biosafety studies and highlight high-impact research areas. These gaps reflect both the breadth of experimental data needed to support evidence-based practices and the broad scope of risks managed by biosafety personnel, which only further underscores the importance of equipping the field with the information necessary to make well-informed decisions. The range of data needs identified falls into three overarching categories:

- Biosafety practices, including the procedures that minimize accidental exposure or release of biological agents;
- Containment infrastructure, including the physical barriers and engineering controls designed to prevent agent escape; and
- Biorisk management systems and personnel, including the organizational policies and processes that implement safe laboratory operations.

Biosafety Practices

Four key themes emerged: agent spread and contamination, exposure prevention, cleaning and decontamination, and waste management. Expert contributors highlighted the need for better data on how biological contamination moves within laboratory environments, including how often contamination occurs, which equipment is most susceptible, and characterization of the types of contamination produced by specific instruments and procedures. Understanding the mechanisms by which research personnel may become contaminated and how these incidents occur was also a top priority. The contributors also called for studies to establish evidence-based practices for personal protective equipment (PPE) selection and use, personnel shower protocols, and hand hygiene tailored to laboratory environments. Related to cleaning and decontamination, contributors called for evidence to guide the optimal frequency of decontamination, the development and validation of decontamination protocols, and a clearer understanding of the effectiveness of chemical and non-chemical methods under various real-world conditions. Despite prior investigations into the reuse of PPE and laboratory consumables after decontamination, more evidence is needed to reliably determine the safety and utility of reuse. Discussions regarding waste management centered on developing strategies to improve adherence to best practices for waste disposal among laboratory staff and parameters for management of carcasses infected with pathogenic agents.

Many laboratories are already conducting studies to verify the effectiveness of their protocols, but these efforts can be time consuming and duplicative, and the findings are not often shared

beyond the institution. There also remain foundational gaps in understanding the type and frequencies of contamination events that could lead to material escaping containment and the efficacy of exposure prevention practices, crucial factors in protecting both the worker and the community. Generating the data identified here, or simply improving access to existing information, would enhance awareness of the greatest risks and hone practices to more effectively and efficiently mitigate them.

Containment Infrastructure

This topic focused on laboratory design and operation, engineering controls and equipment, and verification and certification procedures. Experts highlighted the importance of developing evidence-based global standards for engineering controls, including primary containment devices, laboratory ventilation, and air filtration. They also noted the need for empirical data to guide the appropriate selection, placement, safe and appropriate use, and certification of facility equipment such as steam autoclaves and biosafety cabinets. While various recommendations and some region-specific standards exist for verifying and certifying engineering controls, real-world data is needed to inform how often these procedures are performed and which tests are necessary to ensure ongoing effectiveness. Contributors also emphasized the value of comprehensive life cycle cost analyses to provide the community with a clear understanding of the total expenses of building and operating containment laboratories at all levels. Furthermore, they noted that data related to the selection of construction materials, optimal laboratory sizing and layout, and costs associated with alternative power sources would help inform the design and construction of new containment laboratories that can be maintained safely and sustainably.

The availability of universally accepted, evidence-based standards, or the data and justification used to develop country-specific standards, would allow biosafety professionals to ensure that recommendations are data driven, select those that are appropriate for their use, and understand how to implement them in their unique facilities. This information would also inform efforts to apply proper standards to each unique facility while also ensuring consistent safety across facilities. Similarly, data informing the selection of appropriate facility equipment (e.g., biological safety cabinet [BSC] class based on use case, autoclave size and type, etc.) and its safe and effective use will ensure that research is conducted safely without overengineering of controls. Access to comparative data and real-world performance metrics would empower informed decisions about laboratory construction and operations, resulting in safer and more sustainable facilities. Similarly, sharing life cycle cost data for containment laboratories would enable institutions to conduct more accurate cost analyses for increased efficiency. Addressing these data gaps through new research, data sharing, and standardization would support more informed decision-making, smarter investments, and more resilient laboratory infrastructure, and enhance the overall safety and reliability of containment laboratories.

Biorisk Management Systems and Personnel

Experts raised data needs that centered around the following themes: biorisk management program administration, risk assessment and mitigation, and laboratory personnel and training. For biorisk management systems, contributors emphasized the need for data-driven guidance

on program leadership structures, staffing models, and resource allocation to ensure proper oversight and administration. They also noted gaps in understanding effective approaches to establish and operate biorisk management committees, as well as the frequency and methodology of laboratory inspections. Data are needed to strengthen risk assessments, including determining how often they should be performed and the availability of reliable pathogen-specific inputs, including validated pathogen surrogates. Additionally, there is a need to develop metrics to evaluate the effectiveness of risk control measures once implemented. For personnel and training, experts stressed the need to study human factors that lead to laboratory incidents. They also emphasized the importance of investigating how personnel training can be optimally designed, delivered, and assessed. In addition, there is a need to better understand the factors that contribute to a strong safety culture within a facility, including the behavioral and organizational elements, as well as laboratory stressors.

With robust data, institutions could align their biorisk management programs with proven best practice benchmarks, leading to more consistent and effective oversight. Similarly, standardized data for risk assessments would support the ongoing improvement of safety protocols across laboratories. Data-driven insights on training frequency, delivery methods, and effectiveness would help optimize training programs to better prepare personnel to prevent incidents. Generation of the needed data would enable the design of more effective biorisk management systems, improved risk mitigation strategies, and a safer laboratory culture overall.

How Data can Transform Biorisk Management

Biosafety and research personnel, together with institutional leadership, are essential to safeguarding laboratory workers, public health, and the environment from the biological hazards handled in laboratories. To establish biosafety practices in their facilities, these professionals typically draw on established standards, international best practices, their own experience and expertise, and insights from professional networks. They may also reference a limited set of incident reports or the small body of available quantitative evidence on biorisk mitigation. However, the quantitative data available to biosafety officers is often incomplete, outdated, or not fully tailored to the specific research activities, local context, or unique facility designs they manage. This challenge is especially acute when dealing with emerging pathogens, novel research methodologies, or new laboratory equipment where comprehensive guidance and historical data may be lacking and the associated risks are not yet fully understood. In situations where the level of risk posed by a particular methodology or procedure is unclear, biosafety officers typically default to assuming the highest level of reasonable risk and implementing the most stringent industry standard controls until they are proven unnecessary. While this 'fail-safe' approach prioritizes safety, it can also lead to overengineering and excessive controls, as advances in scientific research often outpace the development of corresponding safety guidance.

When a researcher proposes new work involving a biological agent, a biosafety officer must assess the risks associated with both the agent itself and the procedures used to handle it, then determine appropriate mitigations to reduce those risks. With access to robust evidence on which practices are most effective and under what conditions, biosafety officers could make more informed, context-specific decisions and tailor controls more precisely. This would enable them to implement targeted mitigations (though layering of multiple mitigations may still be warranted), optimize resources, and ultimately create safer, more efficient, and more sustainable environments for biological research. The table below demonstrates how empirical data would assist biosafety officers in assessing present risks and lead to safer laboratory practices. It presents examples of routine risk-reduction practices—including handling biological agents in the BSC, transporting samples, doffing PPE, and hand washing—and summarizes the current basis for each practice, identifies key underlying evidence gaps, and describes how improved data could strengthen effectiveness and reduce accidents.

This Research Agenda outlines numerous needs in biorisk management data that are closely tied to accepted best practices that are currently in place in institutions worldwide. Biosafety officers worldwide want to quantify how effective their current risk mitigation practices are and identify what alternatives may exist to current best practices based on empirical data; these questions are what drives the concepts outlined in this agenda. By strengthening existing practices with empirical data and measurable outcomes, institutions can build a stronger foundation for their site-specific risk assessments. This data-driven approach will provide assurance that mitigation measures effectively protect laboratory staff, their communities, and the environment from the biohazardous material that is being worked with every day.

1

How Evidence Can Strengthen Biosafety. *This table provides examples of routine biosafety practices, the rationale behind them, key evidence gaps, and the types of data that could validate and strengthen their effectiveness.*

Examples of Current Practices		Current Practice Basis	Data Gaps	Potential for Evidence-Based Improvement
 **Work in BSC**	Laboratory personnel work with infectious materials within a certified BSC	International standards, such as the *BMBL* and *LBM*, and industry best practices.[11,12]	Limited empirical data regarding: • Frequency of cross-contamination during pipetting, • Risks of cross-contamination with media of different compositions or viscosities, • Frequency of escape of material from the BSC during pipetting.	• Build on evidence that aerosols generated inside a correctly operating BSC are retained within the cabinet.[11,12] • Investigate workflow adjustments that reduce cross-contamination. • Quantify how rarely spills occur outside the BSC to better inform PPE selections.
 **Sample Transport**	Sealed sample containers are placed in a secondary container with absorbent material, then transported to a freezer.	International standards, such as the *BMBL* and *LBM*, industry best practices, and anecdotal experiences of primary container drops and spills.	Limited empirical data regarding: • How often samples are dropped in a laboratory setting, • How different types of containers may break when dropped, • Characterization of spills when a drop occurs.	• Verify whether cost-effective secondary containers are equally as durable for withstanding drops. • Use incident data to identify whether container drops occur more often in certain areas and establish designated transport routes.
 **PPE Doffing**	Personnel follow a prescribed protocol and order for the decontamination and doffing (i.e., removal) of PPE.	Industry best practices, established routines, existing data from PPE cross-contamination during removal in healthcare settings during outbreaks.	Limited empirical data regarding: • Contamination risks during doffing with a variety of PPE configurations, • Effectiveness of specific doffing sequences and techniques, • PPE removal in a high containment laboratory.	• Leverage findings that healthcare workers often self-contaminate during doffing.[13] • Compare contamination rates across lab-relevant parameters to refine doffing protocols and exit procedures. • Use evidence of effective doffing procedures to improve personnel compliance.
 **Handwashing**	Washing hands with soap and water for at least 20 seconds is required for all personnel after glove removal and before leaving the laboratory.	Universal biosafety standards, general studies on hand hygiene (especially in healthcare settings), some studies on the efficacy of specific soaps/disinfectants on specific pathogens.	Limited empirical data regarding: • Minimum effective duration and technique for handwashing for the range of high consequence pathogens, • Effectiveness of handwashing versus hand sanitizing, or use of both, for specific pathogens.	• Review data on soap/disinfectant efficacy against target pathogens to confirm effective removal. • Identify commonly missed areas during handwashing to redesign effective training and tailor visual reminders in the laboratory.

Navigating the Research Agenda

The Biorisk Research Agenda characterizes the evidence needed to validate and strengthen existing biorisk management practices, as identified by global experts. This agenda spans the life, physical, and social sciences, reflecting the interdisciplinary nature of biorisk management and the diverse expertise required to effectively implement the range of practices.

Data needs are organized into topics and sub-topics within three high-level categories including: (1) biosafety practices, (2) containment infrastructure, and (3) biorisk management systems and personnel. Each identified data need is structured to:

- Contextualize the gap in evidence underlying the indicated biosafety practice,
- Describe factors that are critical to incorporate into the design of studies intended to generate the needed data, and
- Provide examples of basic experiments that could be conducted to address these gaps.

The scope of research needs is broad. Some are straightforward, requiring only basic laboratory equipment and labor hours, while others are complex and necessitate specialized facilities or advanced methodologies. In some cases, relevant data may already exist within institutions that, if made accessible, could accelerate progress and benefit the wider community.

For each data need, notional experimental designs are provided as general examples of how the research questions could be addressed rather than exhaustive or prescriptive protocols. Research teams and implementors of the agenda are encouraged to adapt, expand, and innovate upon these experimental designs as needed. A variety of journal articles, standards, and resources are referenced throughout the agenda to provide supplementary information where relevant and assist potential implementers of the agenda in designing and conducting the necessary research. The inclusion of a particular paper, standard, or guideline is not intended as an endorsement of that document or the country/region that produced it, but rather as a reflection of the information available and suggested by technical experts for a specific topic.

The Biorisk Research Agenda is based on data needs identified by international experts during six project workshops. These sessions were designed to highlight and consolidate high-priority needs for advancing biosafety, resulting in a carefully selected set rather than an exhaustive list. This agenda serves as a starting point, and undoubtedly, additional data needs exist in specific research settings and will emerge as the field evolves. The identified needs are deliberately not ranked or prioritized further, recognizing both the significant value of each topic and the varying capacities of organizations to address them. Addressing any of the data needs outlined in this document will help to strengthen biosafety, and organizations are encouraged to pursue the opportunities most relevant and feasible for their context.

This Research Agenda is designed to support the community in collectively advancing the scientific foundation of biorisk management. Just as the development of this Research Agenda

was a global endeavor, its implementation should similarly reflect international and inclusive collaboration. The wide range of laboratory types and resource levels worldwide should be considered when designing, conducting, and applying biorisk research. Meaningful research can be performed in laboratories with varied equipment, capabilities, and capacities. As such, equitable funding for this work is essential so that laboratories in low- and middle-income countries can be actively involved and research findings represent the breadth of practices and environments.

Realizing the full potential of these proposed studies will require several enabling efforts, including sustainable funding sources, reliable and accessible data sharing mechanisms, and robust global collaboration. Broad uptake and coordinated action among countries and institutions will be key to translating research into practical improvements and harmonizing best practices internationally. With these enabling factors in place, the research outlined in this agenda can drive meaningful and lasting progress in evidence-based biorisk management worldwide.

Appendix: Biorisk Research Agenda

Data Needs and Notional Study Designs for Biosafety Practices

1. Research Opportunities Related to Agent Spread and Contamination

1.1 Data Needs for Contamination of Laboratory Spaces

1.1.1 Factors that influence the risk of contamination along the laboratory operations chain

Contamination can occur in a variety of ways in the laboratory. For example, adulteration of samples may occur when contaminants are inadvertently added to samples during collection, transportation, or analysis, and failure of personnel to change gloves after handling biological agents may lead to contamination of clean working surfaces.[14,15] In both clinical and research laboratories, contamination can lead to inaccurate testing results, extended decontamination procedures, and an overall increase in laboratory costs.[15,16] Despite this, there is little data regarding contamination in the laboratory. Thus, studies are needed to determine the various types of contamination that occur in the laboratory setting and the most effective methods for mitigating these events.

Table 1. Notional Research Design for Contamination Produced by Contamination of a Laboratory Worker's Gloves

Research Goal	To generate data on the rates and types of contamination introduced when a laboratory worker's gloves are contaminated to inform the implementation of effective mitigations
Key Variables	• Biological agent/surrogate type (e.g., bacteria, virus, fungus, etc.) or non-biological tracer (e.g., fluorescent gel) • Sample type (e.g., liquid, gel, solid, etc.) • Specific laboratory practice to be assessed and equipment/supplies used during practice • Sampling method (e.g., swab, rinse, fluorescence under ultraviolet [UV] light, etc.) and scheme (e.g., location on hands, sampling area, etc.) • Mitigation strategies (e.g., frequent glove changes, chemical decontamination of gloves between steps in a procedure, etc.)
Example Protocol	1. Contaminate worker's hands with a realistic amount of fluorescent gel in areas that are most likely to become contaminated during laboratory work (e.g., fingertips, back of hand, etc.). 2. Have individual carry out chosen laboratory activity with samples. 3. After completion of activity, use a UV light to assess samples, equipment, and laboratory surfaces for the presence of contamination. 4. If contamination occurs, implement chosen mitigation strategy and determine efficacy for reducing contamination.
Experimental Outputs	Determination of rates and types of cross-contamination occurring in the laboratory; development of effective mitigation strategies to prevent cross-contamination
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Cherry C et al. (2015) Proof of concept: containment systems that prevent freeze-dryer contamination when lyophilizing Escherichia coli (JM 109). *Drying Technol.* 33 (4)**:** 466-470. • De Lappe N et al. (2009) Role of subtyping in detecting Salmonella cross contamination in the laboratory. *BMC Microbiol.* 9**:** 155. • Farnsworth CW et al. (2020) Evaluation of the risk of laboratory microbial contamination during routine testing in automated clinical chemistry and microbiology laboratories. *Clin Chem.* 66 (9)**:** 1190-1199.

1.1.2 Frequency and causes of laboratory freezer contamination

In most microbiological laboratories, it is common practice to decontaminate surfaces and equipment on a routine basis. However, this may not be the case for the standard (i.e., -20°C) and ultra-low (i.e., -80°C) freezers used for storage of microbial cultures and/or other samples containing biological agents because researchers are hesitant to risk thawing of these frozen materials during transfer to other storage devices without empirical evidence that freezers get contaminated. As such, there is a need for real-world data regarding the rates of contamination of this equipment, the causes of this contamination, and the potential consequences of this contamination to inform the need for and development of effective mitigation strategies and decontamination procedures. Experiments should be carried out in various types of facilities that store different pathogens and sample types. If contamination of freezers occurs, effective decontamination methods should be validated for use with the equipment.

Table 2. Notional Research Design for Laboratory Freezer Contamination

Research Goal	To generate data on the rates and causes of laboratory freezer contamination to inform development of effective mitigation strategies and decontamination procedures
Key Variables	• Biological agent types (e.g., bacteria, viruses, fungi, etc.) and concentrations stored • Sample types (e.g., liquid, tissue, lyophilized powder, etc.) stored • Culture/Sample storage preparation procedure (e.g., type of tube/vessel used, decontamination of tube external surface, etc.) • Storage methodology (e.g., storage in plastic/cardboard boxes, tube racks, etc.) • Frequency of access to stored samples • Sampling method (e.g., swabs, replicate organism detection and counting [RODAC] plates, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.) • Mitigation measures to prevent surface contamination (e.g., surface decontamination of sample tubes, changing gloves before accessing freezer, use of gasketed tubes, etc.) • Chemical disinfectant, decontamination method (e.g., surface wipe or spray down, gas decontamination, etc.) and schedule
Example Protocol	1. Thoroughly decontaminate the freezer to be used for the study. If the freezer has been used for storage of biological agents previously, perform surface sampling to ensure that no viable agents remain. 2. Prepare samples for storage in accordance with laboratory standard operating procedures (SOPs) and store samples in freezer for selected period of time. 3. On the selected schedule, use chosen method to sample tubes, storage boxes/racks, and freezer surfaces for the presence of contamination. 4. If contamination occurs: a) Attempt to determine the cause of the contamination (e.g., leaking tubes, glove contamination, etc.) and implement mitigation strategies intended to prevent contamination from occurring. b) Decontaminate the area using the chosen disinfectant method to remove contamination from surfaces. 5. Use sampling method and scheme to determine efficacy of the chosen mitigation measures and decontamination procedure. a) If contamination continues to occur, adjust mitigation measure and resample until contamination if minimized. b) If viable biological agent remains after decontamination, adjust parameters with the decontamination procedure and re-test until no viable agent remains.

Table 2. Notional Research Design for Laboratory Freezer Contamination	
Experimental Outputs	Rates of contamination of stored materials and freezer surfaces; effective mitigation measures to prevent contamination; development of effective decontamination procedures

1.1.3 Rates of cross-contamination between separate facility spaces

Real-world data regarding the rates and causes of cross-contamination between disparate spaces within research facilities (e.g., other research labs or rooms, non-research "clean spaces, etc.) are needed to inform the development of effective decontamination procedures and mitigation measures that reduce the rates of contamination. Experiments should be carried out in various types of facilities (e.g., plant facility or greenhouse, animal research labs, standard lab space, etc.) and with different pathogens (i.e., bacteria, viruses, and fungi) of plants and/or animals depending upon the facility type. The sampling scheme used should assess for contamination of accessible surfaces in the common area (e.g., floor, walls, etc.) and should be conducted on a set schedule to determine the length of time needed to reach a chosen threshold of contamination that requires decontamination. If contamination occurs, mitigation strategies should be developed and tested to determine if they reduce the rates of cross-contamination. Similarly, different chemical disinfectants and decontamination methods should be tested to identify the best combination for decontamination of the given space.

Table 3. Notional Research Design for Rates of Cross Contamination between Facility Spaces	
Research Goal	To generate data on the rates and causes of cross-contamination between separate areas within research facilities to inform the development of effective mitigation and decontamination procedures
Key Variables	• Facility type • Pathogen type and concentration • Heating, ventilating, and air conditioning (HVAC) system type and parameters for areas being assessed • Sampling method (e.g., RODAC plates, swabs, etc.) and timeline (e.g., daily, weekly, etc.) • Threshold for contamination • Mitigation strategies (e.g., dedicated staff for each room, specific room entry order, full clothing change between rooms, change to pathogen handling procedures, etc.) • Chemical disinfectant • Decontamination method (e.g., surface wipe or spray down, gas decontamination, etc.) and schedule
Example Protocol	1. Develop sampling scheme and use to assess for cross-contamination between spaces on a chosen schedule. 2. Determine the efficacy of chosen mitigation strategies in preventing cross-contamination. 3. Decontaminate the area using the chosen disinfectant and decontamination method. 4. Use previously developed sampling scheme to determine the efficacy of the chose disinfectant and application method.
Experimental Outputs	Rates and types of cross-contamination between separate spaces within research facilities; development of effective mitigation strategies to reduce or prevent cross-contamination; development of decontamination methods and schedules for pathogens used

1.1.4 Rates of pathogen spread within a single plant growth room or greenhouse

Due to space limitations, a single plant growth room or greenhouse may be used to house multiple projects involving different plant pathogens; however, there is a need for experimental data on agent spread within a space to inform this practice. Experiments should be carried out with different pathogen types (i.e., bacteria, viruses, and fungi). If spread of a pathogen occurs, mitigation strategies should be developed and tested to determine their effectiveness in reducing the rates of pathogen spread.

Table 4. Notional Research Design for Rates of Plant Pathogen Spread	
Research Goal	To generate data on the rates of pathogen spread within a plant growth room or greenhouse and efficacy of mitigation strategies
Key Variables	• Pathogen type and mechanism of spread (e.g., airborne, waterborne, direct contact, etc.) • Placement of plants within room • Sampling method (e.g., surface sampling, water sampling, plant sampling, etc.) and timeline (e.g., daily, weekly, etc.) • Mitigation strategies (e.g., placement of physical barriers, workflow adjustments, airflow adjustments, water treatment, assignment of dedicated staff, etc.)
Example Protocol	1. Develop sampling scheme and use to assess for spread of pathogen from infected plants to other matrices (e.g., water, soil, plants, etc.) within the room. 2. Determine the efficacy of chosen mitigation strategies in preventing pathogen spread.
Experimental Outputs	Rates and mechanisms of pathogen spread; development of effective mitigation strategies to prevent agent spread

1.1.5 Rates of pathogen spread between infected animals housed in the same room

Space limitation may also require a single animal housing room to be used for multiple projects involving infected animals; a practice that may lead to pathogen spread when open caging is used. Thus, there is a need for real-world data regarding the rates of pathogen spread among animal hosts within a single animal research space. Experiments should be carried out with different pathogen types (i.e., bacteria, viruses, and fungi) that are transmitted via various routes (e.g., direct contact, aerosol, ingestion, vector-borne, etc.). If spread of a pathogen occurs, mitigation strategies should be developed and tested to determine if they reduce the rates of spread.

Table 5. Notional Research Design for Rates of Animal Pathogen Spread	
Research Goal	To generate data on the rates of pathogen spread between animals housed in the same room and efficacy of mitigation strategies
Key Variables	• Pathogen type and mechanism of spread (e.g., airborne, waterborne, direct contact, etc.) • Arrangement of caging within the room • Sampling method (e.g., surface sampling, water/food sampling, etc.) and timeline (e.g., daily, weekly, etc.) • Mitigation strategies (e.g., placement of physical barriers, airflow adjustments, workflow adjustments, labeling of cages to identify infectious status, etc.)
Example Protocol	1. Develop sampling scheme and use to assess for spread of pathogen from infected animals to other matrices (e.g., surfaces, water, food, etc.) or hosts within the room. 2. Determine the efficacy of chosen mitigation strategies in preventing pathogen spread.
Experimental Outputs	Rates and mechanisms of pathogen spread; development of effective mitigation strategies to prevent agent spread

1.2 Data Needs for Contamination of Laboratory Equipment

1.2.1 Characterization of contamination produced by laboratory equipment during routine use

Previous studies have demonstrated that laboratory equipment that places forces on microbial cultures (e.g., centrifuges, mixers, spectrometers, etc.) can produce infectious aerosols and droplets; however, there is no published method that can be used to assess pieces of lab equipment for production of contamination during routine use.[11,17,18] Lack of a method for assessing contamination produced by lab equipment inhibits its safe use, necessitating that real-world data be generated for use in development of such a method. The developed method should allow users to determine if aerosols/droplets are produced by a given piece of equipment and, if so, characterize the particle size and distribution of the contamination produced.

Table 6. Notional Research Design for Contamination Produced by Laboratory Equipment

Research Goal	To generate data on the production of contamination by pieces of laboratory equipment for use in development of a method for assessing new equipment for production of contamination
Key Variables	• Equipment type • Equipment use parameters (e.g., speed, time, etc.) • Test sample type (e.g., water, uninoculated growth medium, fluorescent dye, microbial culture, etc.) • Test sample housing (e.g., glass/plastic test tube, microcentrifuge tube, microplate, etc.) • Aerosol/droplet sampling method (e.g., particle counter/sizer, microbial settle plates, cassette filters, etc.)
Example Protocol	1. Load appropriate test sample and run chosen equipment under various use parameters. 2. Use aerosol/droplet sampling method to assess for production of contamination. 3. Use data to develop a general method for characterization of contamination production by lab equipment. 4. Validate testing method on various types of equipment under diverse use parameters.
Experimental Outputs	Rates and types of contamination produced by pieces of lab equipment; validated method for assessing lab equipment for production of contamination
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Harper GJ. (1984) Evaluation of sealed containers for use in centrifuges by a dynamic microbiological test method. *J Clin Pathol.* 37 (10)**:** 1134-1139. • Holmes KL. (2011) Characterization of aerosols produced by cell sorters and evaluation of containment. *Cytometry A.* 79 (12)**:** 1000-1008. • Kenny MT, Sabel FL. (1968) Particle size distribution of Serratia marcescens aerosols created during common laboratory procedures and simulated laboratory accidents. *Appl Microbiol.* 16 (8)**:** 1146-1150.

1.2.2 Rates of contamination of equipment used to collect and transport biohazardous waste

In many laboratories, it is common practice to decontaminate surfaces and equipment on a routine basis. However, this may not be the case for equipment that is used to collect and transport biohazardous wastes (e.g., waste bins, carts, etc.). Thus, there is a need for real-world data regarding the rates of contamination of this equipment to inform the development of effective decontamination procedures. Experiments should be carried out in various types of facilities that work with different pathogens (e.g., bacteria, viruses, and fungi) and generate a variety of biowaste

types (e.g., liquids, solids, sharps, carcasses, etc.). Studies should also consider different incident scenarios (e.g., a small hole in a biohazard bag containing waste or transport of waste over poor road conditions, such as pot holes or ruts). If contamination of collection and/or transport equipment occurs, effective decontamination methods should be validated for use with the equipment.

Table 7. Notional Research Design for Contamination of Equipment Used for Collection and Transport of Biohazardous Wastes	
Research Goal	To generate data on the rates of contamination of equipment used for collection and/or transport of biohazardous wastes to inform the development of effective decontamination procedures
Key Variables	• Biological agent types used in laboratory • Equipment type and construction material (e.g., stainless steel, plastic, etc.) • Sampling method (e.g., swabs, RODAC plates, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.) • Chemical disinfectant, decontamination method (e.g., surface wipe or spray down, gas decontamination, etc.) and schedule
Example Protocol	1. Thoroughly decontaminate equipment item and use in typical laboratory workflow. 2. According to the selected schedule (e.g., daily, weekly, etc.), sample equipment and test for the presence of viable biological agent. 3. If contamination occurs, test disinfectants and decontamination methods to identify the best combination for decontamination of the specific item.
Experimental Outputs	Rates of contamination of equipment used for collection and transport of biohazardous waste; development of effective decontamination procedures for equipment

1.2.3 Characterization of contamination of equipment utilized during field studies

Fomites are objects that may become contaminated and transmit a biological agent from one host or place to another.[19] Vehicles, tools, and equipment utilized during field studies involving biological agents may serve as fomites that can transmit the agents between sampling sites and/or to geographic areas not related to the research.[20] These experiments will provide real-world data regarding the rates of contamination of items that could serve as fomites of agricultural pathogens including viruses, bacteria, and fungi that infect plants and animals. Fomites are objects that may become contaminated and transmit a biological agent from one host or place to another.[19] Vehicles, tools, and equipment utilized during field studies involving biological agents may serve as fomites that can transmit the agents between sampling sites and/or to geographic areas not related to the research.[20] These experiments will provide real-world data regarding the rates of contamination of items that could serve as fomites of agricultural pathogens including viruses, bacteria, and fungi that infect plants and animals.

Table 8. Notional Research Design for Contamination of Equipment Utilized During Field Studies	
Research Goal	To generate data on the rates, types, and locations of contamination of vehicles, tools, and other equipment used during field studies involving biological agents
Key Variables	• Biological agent type, concentration, and environmental stability • Fomite type (e.g., vehicle tires, metal tools, shoes, PPE, etc.) • Sampling scheme
Example Protocol	1. Sample potential fomites utilized in field research studies. 2. Use standard microbiological methods to determine the presence of viable biological agent.

Table 8. Notional Research Design for Contamination of Equipment Utilized During Field Studies	
Experimental Outputs	Rates, types, and locations of contamination of potential fomites used in field studies; improved decontamination and transport procedures for equipment during field studies

1.3 Data Needs for Contamination of Laboratory Personnel

1.3.1 Characterization of contamination of research personnel

In the research laboratory, PPE is used in combination with engineering controls to protect personnel from exposure to biological agents. The current edition of *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL)* published by the U.S. Centers for Disease Control and Prevention (CDC) and the U.S. National Institutes of Health (NIH) recommends that PPE be selected based upon a risk assessment of the biological agents and procedures that a lab worker will use.[11] There is a lack of empirical evidence on which to base these risk assessments; thus, there is a need for real-world data regarding the contamination of personnel during work in containment labs/facilities. These data will inform the selection of PPE for specific lab procedures and the need for personnel showers upon exit from high-containment spaces. Studies should be conducted with different pathogen types (i.e., bacteria, viruses, and fungi) and for a variety of common and specialized lab procedures (e.g., pipetting, streaking plates, animal inoculations, etc.).

Table 9. Notional Research Design for Contamination of Research Personnel During Field Studies	
Research Goal	To generate data on the rates, types, and locations of contamination retained on the clothing and/or body of personnel working in research spaces
Key Variables	• Lab/Facility containment level • Biological agent type/concentration or surrogate material • PPE used during research activities • Lab exit and PPE doffing procedures • Sampling methods for various test samples (e.g., hair, skin, clothing, etc.)
Example Protocol	1. Spike samples with chosen agent or surrogate and have personnel carry out chosen procedure(s). 2. Sample personnel for contamination after completion of research activities.
Experimental Outputs	Rates and types of contamination retained on the clothing and body of lab personnel

1.3.2 Contamination of accessories during routine laboratory work

The current edition of the of the *Laboratory Biosafety Manual* (*LBM)* published by the World Health Organization recommends that jewelry be removed prior to working the laboratory if it can be easily contaminated or serve as a fomite.[12] Research has demonstrated that artificial nails, wrist jewelry, and finger rings worn by healthcare workers are often contaminated with microbial pathogens; however, there is little information available about the contamination rates of other accessories (e.g., eyeglasses, hearing aids, earrings, necklaces, false eyelashes, etc.).[21-25] Thus, there is a need for real-world data regarding the rates of contamination of these personal accessories as well as the rates of bodily contamination due to their adjustment (e.g., touching the face while adjusting eyeglasses, touching the arm during wristwatch adjustments, etc.). Experiments should be carried out using different types of samples in a variety of laboratory procedures. If contamination occurs, mitigation

strategies should be developed and tested to determine their effectiveness in reducing contamination of personal accessories.

Table 10. Notional Research Design for Contamination of Eyeglasses During Routine Laboratory Work	
Research Goal	To generate data on the rates of contamination of eyeglasses worn by laboratory personnel during routine procedures and efficacy of mitigation strategies
Key Variables	• Non-biological tracer • Sample type (e.g., liquid, gel, solid, etc.) • Laboratory activity (e.g., processing samples on the benchtop or in a BSC, handling laboratory animals or carcasses, pipetting, etc.) • Sampling method (e.g., swab, rinse, fluorescence under UV, etc.) and scheme (e.g., location on eyeglasses, sampling area, etc.) • Mitigation strategies (e.g., donning of lab goggles over eyeglasses, immediate removal of gloves and handwashing after completion of procedure, various decontamination methods, etc.)
Example Protocol	1. Thoroughly clean and decontaminate eyeglasses prior to start of the chosen lab activity or series of activities. 2. Have individual carry out chosen lab activity using samples spiked with tracer. 3. After completion of activity, sample eyeglasses for contamination. 4. If contamination occurs, implement chosen mitigation strategy, and determine efficacy for reducing contamination of eyeglasses.
Experimental Outputs	Rates of contamination of eyeglasses after specific lab activities; development of effective mitigation strategies to prevent contamination of eyeglasses
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Hedderwick SA et al. (2000) Pathogenic organisms associated with artificial fingernails worn by healthcare workers. *Infect Control Hosp Epidemiol.* 21 (8): 505-509. • Nadikuda S et al. (2011) Effect of finger rings on microbial cross-contamination during dental clinical procedures. IADR General Session 2011. San Diego, CA. • Trick WE et al. (2003) Impact of ring wearing on hand contamination and comparison of hand hygiene agents in a hospital. *Clin Infect Dis.* 36 (11): 1383-1390.

1.3.3 Optimization of PPE doffing order to prevent self-contamination

PPE is worn to provide a barrier between biological agents and the body and/or clothing of the laboratory work handling them.[11] PPE worn for protection from biological agents can range from the use of a lab coat, gloves, and protective eyewear for work with generic microbes or opportunistic pathogens to the use of a full body covering (e.g., coveralls), sometimes covered by a disposable apron or gown, shoe covers or facility-specific footwear, double gloves, protective eye wear, and a respirator when heightened protection is required.[12] The WHO and CDC have published detailed doffing procedures; however, studies have demonstrated that improper doffing of contaminated PPE after use often results in self-contamination.[26-29] For this reason, there is a need for studies that determine how personnel get contaminated during doffing of PPE and then test various doffing orders and mitigations that reduce occurrences of self-contamination. Experiments should be carried out for various PPE ensembles to determine appropriate doffing orders for each.

Table 11. Notional Research Design for PPE Doffing Order to Prevent Self-contamination	
Research Goal	To generate data on how personnel get contaminated during doffing of PPE and test doffing orders and/or mitigations to reduce self-contamination

Table 11. Notional Research Design for PPE Doffing Order to Prevent Self-contamination	
Key Variables	• Training/experience of PPE doffing participants • PPE ensemble (e.g., pieces of PPE worn together) • Doffing order • Biological agent type (e.g., bacteria, virus, fungi, etc.), concentration, and placement or fluorescent gel (e.g., Glo Germ, Dazo Gel, etc.) amount and placement • Location (e.g., fingertips, back of hand, forearms, etc.) and amount of contamination • Method for visualizing and/or measuring contamination (e.g., microbiological plate counts, UV light visualization of fluorescence, etc.) • Mitigations to prevent self-contamination (e.g., revised doffing order, hand hygiene between steps in the doffing procedure, etc.)
	1. Identify PPE ensembles and doffing procedures for testing and identify a cohort of laboratory personnel with experience using each specific PPE ensemble. 2. Have participants don a selected PPE ensemble. 3. Use realistic amounts of fluorescent gel (e.g., droplets, splatter, etc.) to contaminate participants in areas that are likely to become contaminated during routine work. 4. Have the individual remove PPE in accordance with the selected doffing procedure then use a UV light to check for movement of contamination to new locations on the PPE and/or the body of the participant. 6. Once the end point of contamination is determined, implement mitigations intended to prevent self-contamination (e.g., revised order of doffing, hand hygiene between steps in the doffing procedure, etc.) and use UV visualization to determine efficacy of the chosen mitigation measures. 5. Once an effective doffing procedure is determined, validate it by repeating a sufficient number of times.
Experimental Outputs	Evidence based doffing order and/or implementation of mitigations to reduce self-contamination during doffing of PPE
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Chughtai AA, Chen X, Macintyre CR. (2018) Risk of self-contamination during doffing of personal protective equipment. *Am J Infect Control.* 46 (12)**:** 1329-1334. • Liu Y et al. (2024) Contributing risk factors to self-contamination during the process of donning and doffing personal protective equipment. *Disaster Med Public Health Prep*. 18 (1). • Sahay N et al. (2022) Risk of self-contamination because of improper doffing of personal protective equipment: A randomised cross-over study. *Indian J Anaesth.* 66 (9)**:** 638-643.

1.4 Data Needs for Contamination Produced During Laboratory Procedures

1.4.1 Characterization of contamination produced during common laboratory practices

Early studies related to biosafety demonstrated that aerosols and other types of contamination can be produced during common laboratory procedures.[18,30] In recent years, studies have been carried out to quantify and characterize the contamination generated during serial dilution, plating, pipetting, vortex mixing, and homogenization; however, similar data are still lacking for many laboratory procedures.[31-33] Real-world data related to the production of contamination during routine laboratory procedures, including those commonly used in the study of plant or animal pathogens (e.g., plant/animal infection, cage changes, leaf harvesting, use of automated sample handling technologies, etc.), are needed to inform the development or modification of safe lab practices.

Table 12. Notional Research Design for Contamination Produced During Common Laboratory Practices	
Research Goal	To generate data on the rates and types of contamination produced during common laboratory procedures
Key Variables	• Specific laboratory practice assessed and equipment/supplies used during practice • Test sample (e.g., water, fluorescent dye, microbial culture, etc.) • Aerosol/droplet sampling method (e.g., particle counter/sizer, microbial settle plates, cassette filters, etc.) • Human factors related to performance of laboratory practice (e.g., pressure or force used, etc.)
Example Protocol	1. Perform chosen laboratory practice under typical conditions and sample for the creation of contamination. 2. If contamination is produced, develop practice modifications and test for reduction in the rate of contamination.
Experimental Outputs	Rates and types of contamination produced during common laboratory practices; development of practice modifications that reduce or prevent contamination
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Miller HE et al. (2014) Characterization of respirable aerosols generated during routine laboratory procedures. *Appl Biosaf.* 19 (1)**:** 19-27. • Pottage T et al. (2014) Quantification of microbial aerosol generation during standard laboratory procedures. *Appl Biosaf.* 19 (3)**:** 124-131. • Pottage T et al. (2022) Microbial aerosols generated from standard microbiological laboratory procedures. *Appl Biosaf.* 27 (2)**:** 92-99.

1.4.2 Characterization of contamination produced during necropsy of large animals

Necropsy examination of animals presents many hazards due to possible exposure to aerosols and body fluids which may contain biological agents.[34] Necropsy of large animals is especially likely to result in the creation of aerosols and other types of contamination due to the use of powered equipment.[35] Real-world data regarding the levels of contamination produced during necropsy of large animals are needed to ensure the safety of these procedures and to inform the development of effective contamination reduction strategies. Variables tested should include individual variation as well as tool and procedural variation.

Table 13. Notional Research Design for Contamination Produced During Necropsy of Large Animals	
Research Goal	To generate data on the levels and types of contamination produced during necropsy of large animals and develop effective contamination reduction strategies
Key Variables	• Animal species and carcass size • Biological agent type and concentration • Necropsy procedure and tools (e.g., saws, grinders, etc.) • Sampling method (e.g., particle counter/sizer, microbial settle plates, cassette filters, etc.) • Human factors related to performance of laboratory practice (e.g., pressure or force used, etc.) • Contamination reduction strategies (e.g., placement of physical barriers, airflow adjustments, use of different tools, use of a down draft table, etc.)
Example Protocol	1. Perform necropsy using standard techniques and tools while measuring for contamination within the space using the chosen sampling method. 2. Determine the efficacy of chosen contamination reduction strategies.
Experimental Outputs	Rates and mechanisms of contamination produced during large animal necropsy; development of effective contamination reduction strategies

1.4.3 Quantification of aerosols generated during laboratory spills and determination of the need for aerosol settling time before cleanup

It has long been known that infectious aerosols can be generated during spills of biohazardous materials.[36-38] As a result, biohazard spill response protocols often include a 15–60-minute period in which personnel leave the laboratory to allow for these aerosols to settle before cleanup procedures begin.[39,40] Despite this, the aerosols produced by spills and other accidents involving infectious liquids have not been fully quantified and characterized, and it is unclear if the aerosol settling periods specified in spill response protocols are evidence-based. Researchers have quantified and characterized the aerosols produced during small spills of infectious liquids and drops of glassware containing infectious liquids; however, there is a need for additional reps of the these experiments, as well as quantification and characterization of microbial aerosols generated during other spill and laboratory scenarios.[30] If respirable aerosols are generated by a specific spill/incident, experiments should be conducted to determine the need for an aerosol settling period and the length of this period should it be required. Aerosol quantification and characterization experiments should be carried out for a variety of spill/incident types with various pathogen types (e.g., bacteria, viruses, fungi, etc.) in liquids of various volumes and viscosities. Studies related to aerosol settling periods should be conducted under a variety of heating, ventilation, and air conditioning parameters (e.g., air velocity, air changes per hour, etc.) to determine the impact of these factors on the length of time that aerosols remain dispersed in the air.

Table 14. Notional Research Design for Quantification of Aerosols from Laboratory Spills and Determination of the Need for Aerosol Settling Time

Research Goal	To generate data on aerosols generated during biohazard spills and laboratory incidents and the time needed for settling of generated aerosols
Key Variables	• Spill or incident type (e.g., small or large volume spill, dropped agar plate, dropped flask, etc.) • Biological agent/surrogate type and concentration • Liquid viscosity and volume • HVAC parameters • Aerosol sampling device (e.g., particle counter/sizer, cyclone sampler, slit sampler, Andersen sampler, etc.) and operation parameters (e.g., placement, volume of air sampled, operation times, etc.) • Total sampling time (e.g., 30 minutes, 60 minutes, etc.)
Example Protocol	1. Create spill/incident while using selected sampling device(s) to measure the total number of particles generated and the size distribution of the microbial aerosol. 2. Continue sampling on a selected schedule (e.g., every 10 minutes) to determine the time required for the aerosol to settle out of the air. 3. Use data to develop an evidence-based recommendation for time needed to allow aerosols to settle before commencing cleanup procedures.
Experimental Outputs	Quantification and characterization of aerosols generated by a specific spill/incident type; evidence-based aerosol settling time
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Bennett A, Parks S. (2006) Microbial aerosol generation during laboratory accidents and subsequent risk assessment. *Appl Microbiol.* 100 (4)**:** 658-663. • Kenny MT, Sabel FL. (1968) Particle size distribution of Serratia marcescens aerosols created during common laboratory procedures and simulated laboratory accidents. *Appl Microbiol.* 16 (8)**:** 1146-1150.

1.4.4 Contamination of wastewater via laboratory sinks and survivability of pathogens in wastewater streams

In most global regions, liquids containing biological agents are decontaminated with an appropriate chemical disinfectant before being introduced into the municipal sewer unless the sewer is attached to an advanced waste treatment plant.[12,41] Despite precautions, accidental disposal of untreated waste or handwashing in biological laboratories can introduce pathogens into the sewer system which may pose risks in areas lacking advanced wastewater treatment facilities or where wastewater is reused, with or without treatment, for agricultural purposes.[42] Thus, studies are needed to determine the degree to which pathogens enter wastewater via laboratory sinks and to assess the survivability of pathogens in wastewater streams to understand the degree of risk associated with reuse of untreated wastewater. Experiments performed to assess the survivability of agents in wastewater should include use of a variety of biological agents (e.g., bacteria, viruses, fungi, etc.) in relevant concentrations to account for any impacts the pathogen type may have.

Table 15. Notional Research Design for Contamination of Wastewater via Laboratory Sinks

Research Goal	To generate data on the contamination of wastewater via laboratory sinks
Key Variables	• Type and concentration of biological agents used in laboratory • Availability and type of wastewater treatment • Method for measuring entry of agents into the wastewater stream (e.g., effluent sampler placed before lab wastewater mixes with wastewater stream, collection of sink waste in diversion tank for sampling, filtration of all sink wastewater followed by testing of filter, etc.) • Frequency of sink use • Frequency of sampling • Length of study (e.g., six months, one year, etc.)
Example Protocol	1. Identify two buildings (one that houses laboratories and one that does not) for an initial study to obtain a baseline. 2. Collect wastewater output from each building and use standard microbiological techniques to determine the microbial load in the wastewater from each building. a) A baseline contamination level from the laboratory building that is not significantly higher than the non-laboratory building indicates that the laboratory contribution is not meaningful, and additional investigation is not necessary. b) A significantly higher microbial load in wastewater from the laboratory building indicates that the laboratories may be contributing to contamination of wastewater and additional studies should be conducted as described below. 3. Identify a cohort of laboratories that perform studies with various types of biological agents to participate in the study. 4. Outfit sinks with diversion tanks to collect the wastewater from each sink. 5. Collect wastewater from tanks on a selected schedule (e.g., daily or weekly) over the study period. For each wastewater batch, obtain a representative sample then use standard microbiological techniques to recover and enumerate all biological agents present. 6. At the end of the study period, aggregate data to determine the types and amounts of microbial contamination that laboratories introduce into wastewater streams on an annual basis.
Experimental Outputs	Types and amounts of microbial contamination that laboratories introduce into wastewater streams annually

Table 16. Notional Research Design for Survivability of Pathogens in Wastewater Streams	
Research Goal	To generate data on the survivability of pathogens in wastewater
Key Variables	• Biological agent type and concentration • Wastewater components (e.g., organic matter, suspended solids, nutrients, chemicals, etc.) and conditions (e.g., pH, temperature, aeration, etc.) • Sampling method and schedule (e.g., daily, weekly, etc.) • Length of study (e.g., six months, one year, etc.)
Example Protocol	1. Design a selective culture mechanism to recover the biological agent of interest from a microbe-rich matrix. 2. Collect samples from various municipal wastewater streams and introduce selected biological agent at a relevant concentration based on data obtained in the above experiment and incubate in conditions typical for the wastewater stream being tested. 3. On the selected schedule, obtain a representative sample from each inoculated wastewater sample and use the selective culture method to recover and enumerate the target biological agent. 4. Continue testing for presence of the target agent on the select schedule until the agent is no longer present or the chosen endpoint of the study is reached. 5. Use data to inform the need for antimicrobial treatment of wastewater before reuse.
Experimental Outputs	Survivability of biological agents in wastewater; evidence-based recommendation regarding the need for antimicrobial treatment of wastewater before reuse
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Li J et al. (2015) Retention in treated wastewater affects survival and deposition of Staphylococcus aureus and Escherichia coli in sand columns. *Appl Environ Microbiol.* 81 (6)**:** 2199-2205. • Murphy H. (2017) Persistence of Pathogens in Sewage and Other Water Types. In *Water and Sanitation for the 21st Century: Health and Microbiological Aspects of Excreta and Wastewater Management (Global Water Pathogen Project)*. Rose JB, Jiménez-Cisneros B (eds.). E. Lansing, MI: Michigan State University. • Panda B, Chidambram S, Malakar A. (2021) Survival of SARS-CoV-2 in Untreated and Treated Wastewater - A Review. In *Environmental Resilience and Transformation in Times of COVID-19: Climate Change Effects on Environmental Functionality* Ramanathan AL et al (eds.). Amsterdam, Netherlands: Elsevier. • Ye Y et al. (2016) Survivability, partitioning, and recovery of enveloped viruses in untreated municipal wastewater. *Environ Sci Technol.* 50 (10)**:** 5077-5085.

2. Research Opportunities Related to Exposure Prevention

2.1 Data Needs for PPE

2.1.1. Selection of PPE during field studies

In the research laboratory, PPE is used in combination with engineering controls to protect personnel from exposure to biological agents. The use of appropriate PPE during field work involving biological agents may be especially important because it is the only barrier between the wearer and the agents in the absence of engineering controls such as a BSC.[11] Additionally, in field studies involving agricultural pathogens that do not infect humans (i.e., plant or non-zoonotic animal pathogens), PPE may play an important role in preventing the transmission of these agents among research sites or to

other environmental locales on the body or clothing of the researchers. Unfortunately, the use of PPE is not often incorporated into the design of field studies.[43] Thus, there is a need for data regarding the rates of contamination of research personnel during field studies involving biological agents to inform the selection and use of appropriate PPE. Studies should be conducted with viral, bacterial, and fungal pathogens to account for any impacts the pathogen type and host may have.

Table 17. Notional Research Design for Selection of PPE During Field Studies

Research Goal	To generate data on the rates and types of contamination retained on the clothing and/or body of personnel taking part in field studies involving biological agents
Key Variables	• Biological agent type, concentration, and route of exposure • Host type (e.g., crop plants, livestock, wild animals, etc.) • Sampling methods for various test samples (e.g., hair, skin, clothing, etc.) • PPE use procedures (e.g., PPE types needed, doffing procedures, waste processing, etc.)
Example Protocol	1. Sample personnel for contamination after completion of field research activities. 2. Evaluate frequency, amount, and location of contamination per activity type. 3. Develop appropriate PPE use procedures. 4. Test for reduction in the rates of personnel contamination due to PPE use.
Experimental Outputs	Rates and types of contamination retained on the clothing and body of research personnel during field studies; development of appropriate PPE use procedures

2.1.2. Selection of PPE during laboratory studies

In the research laboratory, PPE is used in combination with engineering controls to protect personnel from exposure to biological agents. The current edition of the *LBM* published by the WHO recommends that the PPE chosen for use in a laboratory study be selected based upon the results of a risk assessment that considers the biological agent(s) used in the study as well as the procedures conducted and/or the laboratory equipment used.[12] Although there are data on PPE failure rates and cross contamination in the hospital setting, data related to similar situations in the laboratory are missing, making it difficult to conduct an evidence-based risk assessment. Thus, there is a need for data regarding the rates of contamination of research personnel during laboratory procedures involving biological agents to inform the selection and use of appropriate PPE. Studies should be conducted with viral, bacterial, and fungal pathogens to account for any impacts the pathogen type may have and should begin with high-risk procedures (e.g., necropsy of large animals, handling of carcasses infected with biological agents, flaming of inoculation loops, etc.).

Table 18. Notional Research Design for Selection of PPE for Laboratory Studies Involving Biological Agents

Research Goal	To generate data on the rates and types of contamination retained on the clothing and/or body of personnel taking part in laboratory studies involving biological agents
Key Variables	• Biological agent type (e.g., bacteria, virus, fungus, etc.), form (e.g., bacteria in liquid culture, fungus on agar plate, etc.), concentration, route of exposure • Laboratory procedure(s) conducted and equipment (e.g., vortex mixer, centrifuge, etc.) used • Sampling methods for various test samples (e.g., hair, skin, clothing, etc.) • PPE use procedures (e.g., PPE types needed, doffing procedures, waste processing, etc.)
Example Protocol	1. Sample personnel for contamination after completion of laboratory research activities. 2. Evaluate frequency, amount, and location of contamination per activity type. 3. Develop appropriate PPE use procedures. 4. Test for reduction in the rates of personnel contamination due to PPE use.

Table 18. Notional Research Design for Selection of PPE for Laboratory Studies Involving Biological Agents	
Experimental Outputs	Rates and types of contamination retained on the clothing and body of research personnel during laboratory studies; development of appropriate PPE use procedures

2.1.3. Efficacy of PPE during field studies

The use of appropriate PPE during field work involving biological agents may be especially important because it is the only barrier between the wearer and the agents in the absence of engineering controls such as a BSC.[11] In addition to protecting personnel from pathogens, the use of PPE during field studies involving agricultural pathogens may play an important role in preventing the transmission of these agents among research sites or to other environmental locales on the body or clothing of the researchers. PPE used during field studies should be chosen based on a risk assessment of all potential hazards associated with the study, such as exposure to infectious agents and/or hazardous chemicals, animal and insect use, and use of sharps. However, the selection of PPE to mitigate these risks may be difficult due to environmental factors.[43-45] For example, the use of isolation gowns and latex or nitrile gloves may present durability issues, but the use of durable PPE such as leather gloves and canvas coveralls may be problematic due to their permeability. Thus, there is a need for data regarding the efficacy of PPE items made of various materials for use in field research studies. PPE of various types should be tested for its ability to provide adequate protection and its durability under typical study conditions.

Table 19. Notional Research Design for Efficacy of PPE During Field Studies	
Research Goal	To generate data on the efficacy of PPE used in specific applications during field studies
Key Variables	• Study type (e.g., animal use, chemical use, etc.) • Biological agent type and concentration • Experimental procedures (e.g., animal/plant sampling, use of tools, etc.) • Sampling methods for biological agent of interest • PPE type (e.g., gloves, body covering, footwear, eye protection, etc.) • PPE compatibility with chemicals used in study (e.g., disinfectants, pesticides, etc.)
Example Protocol	1. Select PPE for the given study and have personnel wear PPE items while conducting study activities. 2. Assess protective power of PPE items by sampling personnel for contamination by pathogen of interest after doffing of PPE. 3. Assess durability of PPE for use in study activities by observing for holes, tears, or other forms of failure. 4. Assess for chemical compatibility by exposing PPE to the chemical of interest and observing of forms of failure as above.
Experimental Outputs	Recommendations for PPE use during field studies

2.2 Data Needs for Personnel Showers

2.2.1. Evidence base for personnel showers upon laboratory exit

In the context of biosafety, showers for laboratory personnel are intended to serve as a secondary barrier to reduce the potential for loss of containment due to carriage of a pathogen out of a facility on a person's body. The current edition of the *BMBL* requires that personnel take showers upon exit

from BSL-4, ABSL-4, and ABSL-3Ag labs/facilities and recommends that risk assessments be used to inform the need for personal showers upon exit from BSL-3, ABSL-3, and ABSL-2Ag labs/facilities.[11] However, the recommendations for full-body showers upon exit from these high- and maximum-containment laboratories does not appear to be based on scientific evidence. As such, there is a need for real-world data regarding how often the underclothing and bodies of personnel become contaminated when working in one of these laboratories. Studies should be carried out in laboratories/facilities of different levels using PPE ensembles, sample types, and laboratory procedures relevant to each level. These data will determine how often individuals become contaminated when working in these laboratories and, thus, will inform the need for personnel showers to remove such contamination.

Table 20. Notional Research Design for Evidence Base for Personnel Showers

Research Goal	To generate data on the rate of contamination of personnel upon exit from high- and maximum-containment laboratories to inform the need for personal showers
Key Variables	• Laboratory/facility type (e.g., standard laboratory, animal facility, etc.) and level (i.e., CL, PC, BSL, ABSL, etc.) • PPE ensemble worn during lab work (e.g., coveralls with built-in shoe covers and powered air purifying respirator [PAPR] with hood, positive pressure suit, etc.) • Biological agent/surrogate type (e.g., bacteria, virus, fungi, etc.) and concentration or non-biological tracer • Type of sample(s) manipulated in lab (e.g., liquids, agar plates, animal tissues, etc.) and procedures conducted • Sampling methods for various test samples (e.g., fabrics, hair, skin, etc.)
Example Protocol	1. Have a qualified laboratorian don appropriate PPE, enter the selected laboratory, and perform the chosen procedures using the selected sample type spiked with fluorescent dye. 2. When procedures are complete, have the laboratorian exit the laboratory and doff PPE in accordance with the laboratory's standard exit procedure. 3. After PPE is doffed, use a UV light to examine the under clothing and body of the laboratorian for contamination by the fluorescent dye. 4. Repeat a sufficient number of times to calculate the rates of contamination of the personnel upon exit from high- and maximum-containment laboratories/facilities.
Experimental Outputs	Rate of contamination of personnel upon exit from high- and maximum-containment laboratories; evidence-based recommendation for personal shower requirements
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Amlôt R et al. (2010) Comparative analysis of showering protocols for mass-casualty decontamination. *Prehosp Disaster Med*. 25 (5): 435-439. • Chilcott RP, Larner J, Matar H. (2019) UK's initial operational response and specialist operational response to CBRN and HazMat incidents: a primer on decontamination protocols for healthcare professionals. *Emerg Med J*. 36 (2): 117-123. • Collins S et al. (2021) Mass casualty decontamination for chemical incidents: research outcomes and future priorities. *Int J Environ Res Public Health*. 18 (6): 3079. • Collins S, et al. (2021) Evaluating the impact of decontamination interventions performed in sequence for mass casualty chemical incidents. *Sci Rep.* 11(1):14995.

2.2.2. Parameters for personnel shower procedures

In the context of biosafety, showers for laboratory personnel are intended to serve as a secondary barrier to reduce the potential for loss of containment due to carriage of a pathogen out of a facility on a person's body. However, the showering process may increase the risk of worker infection because the pathogen may be aerosolized or spread to other parts of the body. The current edition of the *BMBL* recommends that personnel take showers upon exit from BSL-4, ABSL-4, and ABSL-3Ag labs/facilities and recommends that risk assessment be used to inform the need for personnel showers upon exit from BSL-3, ABSL-3, and ABSL-2Ag labs/facilities.[11] However, there is very little evidence to support the implementation of personnel shower requirements. There is a need for real-world data regarding what happens to the pathogen when a contaminated worker takes a personnel shower (e.g., is the pathogen aerosolized or moved to other body parts, does soap inactivate it, etc.) and what specific shower procedures (e.g., shower length, water temperature, detergent use, etc.) are needed to remove the material safely. These data will inform the utility of personnel showers and can be used to refine personnel shower procedures.

Table 21. Notional Research Design for Evidence-Based Personnel Shower Procedure

Research Goal	To generate data on the fate of contaminating microorganisms during the personnel shower process and develop effective shower procedures for pathogen removal and/or inactivation
Key Variables	• Laboratory containment level • Biological agent/surrogate type and concentration • Location (e.g., body part) and amount of contamination • Sampling methods for various test samples (e.g., hair, skin, water, shower surfaces, drains, air etc.) • Shower parameters (e.g., water temperature, shower length, etc.) • Shower procedures (e.g., washing order, detergent used, etc.)
Example Protocol	1. Contaminate an individual or manikin with the chosen pathogen (manikin) or surrogate (individual). 2. Use the chosen sampling procedure to trace the spread of the contaminant during the personnel shower process. 3. Develop and test personnel shower procedures that safely remove or inactivate the organism.
Experimental Outputs	Development of effective personnel shower procedures

2.3 Data Needs for Hand Hygiene

Studies show that the hands of healthcare workers are the primary vector for pathogens in healthcare settings, and thus, hand hygiene is the foundation of infection control programs in hospitals and other health-related facilities.[46-49] Due to the importance of this transmission mechanism, hand hygiene guidelines have been developed for use in healthcare settings.[50,51] Despite the use of biological agents in research and teaching laboratories, little research has been done to develop hand hygiene parameters and guidelines that are specific to these environments; instead, the hand hygiene procedures developed for use in healthcare are utilized in these laboratories without modification.[11,12]

2.3.1 Frequency of hand hygiene for laboratory personnel

Current editions of the *BMBL* and the *LBM* recommend hand washing or sanitization after un-gloved contact with contaminated materials, after removal of gloves, after completion of work with biohazardous materials, and prior to leaving the laboratory.[11,12] While logical, this recommended frequency of hand hygiene is not based on evidence about when and how often material contaminates the hands, so it is possible that hands should be washed more often than currently recommended. As such, there is a need for real-world data regarding how often the hands of laboratory personnel become contaminated to inform an evidence-based recommendation for the required frequency of hand hygiene. Studies should be conducted both with and without gloves and with a variety of laboratory activities that may result in contamination of the hands.

Table 22. Notional Research Design for Frequency of Hand Hygiene

Research Goal	To generate data on the rates of contamination of the hands of laboratory personnel after lab activities to inform the required frequency of hand hygiene
Key Variables	• Non-biological tracer • Laboratory activity type (e.g., handling high-concentration microbial cultures, animal necropsy, pipetting, etc.) • Sampling method (e.g., swab, rinse, fluorescence under UV, etc.) and scheme (e.g., location on hand, sampling area, etc.) • Use of appropriate gloves for lab activities
Example Protocol	1. Thoroughly decontaminate hands of individual prior to start of chosen lab activity or series of activities. 2. Have individual carry out chosen lab activity using samples spiked with the tracer. 3. Sample individual's hands for contamination after completion of each activity.
Experimental Outputs	Rates of contamination on the hands of laboratory personnel after specific lab activities; evidence-based hand hygiene frequency recommendations for laboratory personnel
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Montville R, Chen Y, Schaffner DW. (2001) Glove barriers to bacterial cross-contamination between hands to food. *J Food Prot.* 64 (6)**:** 845-849. • Traub-Dargatz JL et al. (2006) Pilot study to evaluate 3 hygiene protocols on the reduction of bacterial load on the hands of veterinary staff performing routine equine physical examinations. *Can Vet J.* 47 (7)**:** 671-676. • Wyneken H et al. (2023) Frequency of leaks from conical centrifuge tubes. *Appl Biosaf.* 29 (1): 1-9. • Wyneken HL et al. (2023) Rate of splashes when opening microfuge tubes with various methods. *Appl Biosaf.* 28 (2)**:** 123-129.

2.3.2 Standardization of variables & methods used in handwashing studies and advancing understanding of the chemical & physical nature of skin-microbe interactions

Researchers have conducted thousands of studies regarding the procedures for and efficacy of handwashing; however, variation in the methodologies used can impede comparison of these studies. Thus, there is a need for standardization of the variables involved in the handwashing procedure as well as the test methods used in studies of handwashing.[52] Studies related to this need will involve a thorough review of the literature, to determine those variables that should be included in studies and the various methods that are available for use in those studies, followed by laboratory experimentation to determine those methods and variable values to be used in handwashing studies moving forward.

Additionally, there is a need for studies that provide foundational information about the interaction of microorganisms with the skin of the hands and the materials used in hand hygiene processes (e.g., detergents, hand sanitizing chemicals, water, etc.) to inform the design of reproducible experiments related to hand washing and/or hand sanitization. Needs related to this topic include, but are not limited to, information regarding how microbes interact with detergents during hand washing, what characteristics of a pathogen (e.g., presence of a viral envelope or bacterial capsule, etc.) impact the applicability of handwashing, and development of synthetic materials that accurately mimic the behavior of biological agents on the hands during hand hygiene practices. Due to the broad nature of this need, we expect that related hypotheses will be developed and tested by researchers with expertise in a variety of disciplines, including chemistry, physics, and materials science.

Table 23. Notional Research Design for Standardization of Variables and Test Methods for Handwashing Studies

Research Goal	Standardization of the variables and test methods used in handwashing studies to allow for effective comparison of study results
Key Variables	• Biological agent/surrogate type (e.g., bacteria, virus, fungi, etc.) or non-biological tracer • Factors involved in the handwashing process (e.g., soap type, amount of water used, water flow rate, duration of handwashing, drying method, etc.) and associated variables (e.g., amount of soap used, water temperature, etc.) • Technique for hand inoculation (e.g., natural contamination, palm or finger inoculation, etc.) and associated variables (e.g., initial agent concentration, etc.) • Microbe recovery method (e.g., swabbing, glove juice method, etc.) and associated variables (e.g., reagents used, buffer/solution volume, wet vs. dry swab sampling, application time, etc.)
Example Protocol	1. Review previous studies to determine the factors and associated variables that have the greatest impact on handwashing efficacy and determine optimum values for each factor to be used in future handwashing studies (e.g., amount of soap used, water temperature range, handwashing time, etc.). 2. Review previous studies to determine the available methods for inoculation of the hands. Determine methods that allow for control of various variables leading to consistent application among studies. Determine optimum values for each variable (e.g., amount of inoculum transferred to hands, location of inoculum on the hands, etc.) included in the selected methods. 3. Review previous studies to determine the available methods for recovery of microbes from the hands. For each method, determine the reagents and specific steps or procedures that should be used in future handwashing studies. 4. Publish standardized variables and test methods for use in future handwashing studies.
Experimental Outputs	Standardized variables and test methods for use in handwashing studies
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • British Standards Institute. (2000) BS EN 1499:2013 Chemical Disinfectants and Antiseptics. Hygienic Handwash (Phase 2, Step 2 test). London, England: British Standards Institute. • Conover DM, Gibson KE. (2016) A review of methods for the evaluation of handwashing efficacy. *Food Control.* 63**:** 53-64. • Schürmann W, Eggers HJ. (1985) An experimental study on the epidemiology of enteroviruses: water and soap washing of Poliovirus 1 – contaminated hands, its effectiveness and kinetics. *Med Microbiol Immunol*. 174: 221-236.

3. Research Opportunities Related to Sample Packaging and Storage

3.1 Data Needs Related to Sample Packaging

3.1.1. Decontamination of external packaging and impact on performance

Many countries adhere to country-specific or international regulations that govern the transport of biological agents via air. For example, many countries and industry groups follow, in full or in part, regulations governing the transport of infectious materials by air, including those set forth by the UN's International Civil Aviation Organization (ICAO) and the International Air Transport Association (IATA).[11] The IATA Dangerous Goods Regulations provide instructions for packaging of infectious substances for shipping based on the risks associated with infection by the specific organism. Under these regulations, both Category A and Category B biological substances must be shipped in triple packaging that consists of a sealed primary container, secondary packaging (leakproof secondary packaging required for some infectious substances), and a rigid outer package capable of withstanding specific performance tests.[11,53] Due to these requirements, purpose-made packaging materials intended for shipping of infectious substances can be costly and are often reused for subsequent shipping of biological materials. Thus, there is a need for studies to inform the safe reuse of these materials. First, studies should aim to determine if decontamination of these materials is necessary by providing real-world data regarding how often packaging materials become contaminated during the shipping process. If it is determined that these materials become contaminated, disinfection and reuse of porous packaging items (e.g., cardboard, polystyrene foam, paper canisters, etc.) required for shipping of infectious materials must be tested. Experiments should be conducted with variety of packaging materials and various decontamination methods (e.g., exposure to vaporized hydrogen peroxide or other chemical disinfectants, heat/steam treatment, UV irradiation, etc.) to identify an effective and feasible method for decontamination of these shipping materials. These studies should also assess the impact of the decontamination method on the integrity and performance of the packaging materials to determine the number of decontamination and reuse cycles that each item can undergo before performance is lost. Finally, if an effective and non-damaging decontamination method is identified for a given packaging type, a techno-economic analysis should be conducted to ensure that decontamination and reuse of the packaging produces the desired cost savings.

Table 24. Notional Research Design for Frequency of Contamination of Packaging Materials

Research Goal	To generate data on the rates of contamination of secondary and tertiary packaging used in the shipping of biological agents to inform the need for decontamination of packaging materials before reuse
Key Variables	• Biological agent/surrogate type (e.g., bacteria, virus, fungus, etc.) or non-biological tracer • Sample form (e.g., liquid, solid, tissue, etc.) • Primary container type (e.g., screw-top tube, flip-top tube, etc.) • Secondary/Tertiary packaging material (e.g., cardboard box, paper canister, polystyrene foam, etc.) • Packer/shipper training and experience • Sampling method (e.g., swab, RODAC plate, fluorescence under UV, etc.) and scheme (e.g., location of sampling, number of samples, etc.) • Total number of packages tested

Table 24. Notional Research Design for Frequency of Contamination of Packaging Materials	
Example Protocol	1. When a package containing a biological agent is received, unpack carefully to access all packaging components. 2. Use the selected method to sample each packaging material for the presence of the target biological agent or non-biological tracer. 3. Once a sufficient number of packages have been tested, calculate the rate of contamination of each packaging material.
Experimental Outputs	Rates of contamination of secondary and tertiary packaging used in the shipping of biological agents

Table 25. Notional Research Design for Decontamination of Packaging Materials for Reuse	
Research Goal	To generate data on the decontamination of packaging materials and impacts of decontamination procedures on performance of the materials during reuse
Key Variables	• Biological agent or surrogate organism type and concentration • Target packaging material(s) (e.g., cardboard, polystyrene foam, absorbent materials, shipping canisters etc.) • Performance metrics for each material (e.g., rigidity of cardboard, watertightness of canisters, integrity of polypropylene foam, etc.) and testing methodologies • Decontamination method and parameters (e.g., chemical concentration, temperature, exposure time, etc.) • Number of decontamination and reuse cycles • Sampling method and scheme
Example Protocol	1. Contaminate packaging materials with a known concentration of the target biological agent(s) or surrogate(s). 2. Expose the contaminated material to the selected decontamination methods using various parameters. 3. Attempt to recover the target organism or surrogate to determine protocol parameters that effectively kill the target organism. 4. Once an effective decontamination protocol is developed, repeat the decontamination procedure on the material, assessing performance of the item after each decontamination cycle, until performance of the material falls below the acceptable threshold. 5. Validate the decontamination protocol efficacy and appropriate reuse conditions by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for decontamination and reuse of packaging materials intended for use in shipping of infectious materials
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Calfee MW et al. (2016) Evaluation of standardized sample collection, packaging, and decontamination procedures to assess cross-contamination potential during Bacillus anthracis incident response operations. *J Occup Environ Hyg*. 13 (12): 980-992. • Fadiji T et al. (2018) Mechanical design and performance testing of corrugated paperboard packaging for the postharvest handling of horticultural produce. *Biosyst Eng*. 171: 220-244. • Sánchez JH, Gouveia S, Cameselle C. (2022) Transport of high-risk infectious substances: packaging for the transport of category A infectious specimens in Spain. *Int J Environ Res Public Health*. 19 (20). • Sek MA. (1996) A modern technique of transportation simulation for package performance testing. *Pack Tech Sci*. 1996. 9: 327-343.

3.1.2. Appropriate packaging for transport of samples containing biological agents

Many countries have implemented regulations which govern the international transport of biological agents by air, rail, road, and/or sea while other countries have no enforceable regulations for the transport of these materials.[11,54] Purpose-made biological agent shipping containers that satisfy these standards may not be readily available or attainable due to resource restrictions in areas without transport regulations, so there is a need for data regarding the containment efficacy of the non-traditional packaging materials that may be used in these locales. Model regulations prepared by the United Nations (UN) Economic and Social Council (UN ECOSOC) recommends that biological agents belonging to Category A (i.e., those with the potential to cause permanent disability, life-threatening illness, or death in healthy adult humans and/or other animals) and Category B (i.e., those not in category A) be transported in packaging that passes different specified performance tests that ensure adequate containment.[55] Studies that test the ability of non-traditional packaging to pass these performance tests should be conducted to identify off-label packaging that can safely contain biological material during transport.

Table 26. Notional Research Design for Containment Efficacy of Non-Traditional Packaging for Transport of Biological Agents

Research Goal	To generate data on the efficacy of non-traditional packaging for containment of biological agents during transport to inform the development of effective sample transport procedures
Key Variables	• Agent category (i.e., A or B) handled and typical sample types (e.g., liquid, solid, gel, etc.) • Packaging materials (e.g., sealed plastic bag, cardboard box, snap-top storage container, personal cooler, etc.) [55] • Performance tests (e.g., drop test, internal pressure test, water spray test, etc.)
Example Protocol	1. Collect non-traditional packaging materials used during transport of biological agents. 2. Perform relevant performance tests for the given agent category in accordance with recommendations.[55] 3. Develop transport procedures that utilize only those non-traditional packaging materials that pass performance testing.
Experimental Outputs	To generate data on the efficacy of non-traditional packaging for containment of biological agents during local transport; evidence-based development of effective sample transport procedures
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • United Nations. (2023) *Recommendations on the Transport of Dangerous Goods - Model Regulations*. Vol., 23rd revised edn. New York and Geneva: United Nations Publications. • Robinson J et al. (2025) Infectious Sample Transport: Evaluating the Use of Parafilm for Sealing Primary Containers. *Appl Biosaf*. 30 (1): 11-18.

3.1.3. Frequency of sample rejection due to improper packaging

Proper packaging of samples submitted for clinical/diagnostic testing is necessary to ensure the integrity of samples for testing and the safety of transportation and laboratory personnel.[56] Packaging recommendations have been developed for use with samples submitted to clinical medicine and veterinary diagnostic testing laboratories; yet, improper packaging continues to be a major cause of sample rejection for laboratories that perform this testing.[56-59] Thus, there is a need for data regarding the frequency with which clinical/diagnostic samples are rejected due to improper packaging and the specific reasons for the rejection. These data will inform the development of

effective mitigation measures that prevent the rejection of samples due to packaging issues and may also be used in the design of improved packaging.

Table 27. Notional Research Design for Frequency of Sample Rejection due to Improper Packaging	
Research Goal	To generate data on the rates of clinical/diagnostic sample rejection due to improper packaging to inform the development of effective mitigations
Key Variables	• Sample type (e.g., liquid, tissue, semi-solid, etc.) • Packaging type (e.g., tube, plastic bag, snap top container, cardboard box, etc.) • Type of improper packaging (e.g., unsealed primary container, lack of secondary and/or tertiary container, absence of absorbent material for liquid samples, etc.) • Mitigation measures (e.g., training of clinical personnel to properly package samples, distribution of sample packaging kits with pictorial instructions, etc.) • Study length and number of samples received during study period
Example Protocol	1. Assess all samples received during the study period to determine the frequency of samples rejected due to improper packaging and the specific types of improper packaging. Document the specific reason for rejection. 2. Implement mitigation measures for each type of improper packaging. 3. Determine efficacy of mitigation measures by reassessing samples received over a given period for improper packaging. 4. If improperly packaged samples are still received, adjust mitigations and reassess until improper packaging of samples is minimized.
Experimental Outputs	Rates of sample rejection due to improper packaging for a specific clinical/diagnostic laboratory; specific reasons for rejection due to packaging; development of effective mitigation strategies to prevent improper packaging
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Shiferaw MB, Yismaw G, Getachew H. (2018) Specimen rejections among referred specimens through referral network to the Amhara Public Health Institute for laboratory testing, Bahir Dar, Ethiopia. *BMC Res Notes.* 11 (1)**:** 781.

3.2 Data Needs for Biological Agent Inventory

3.2.1. Efficacy of biological agent inventory modalities

Current editions of the *BMBL* and the *LBM* recommend implementation of biological agent inventory procedures to track materials held in the laboratory and to discourage theft or misuse of the materials.[11,12] There are a variety of methods, ranging from handwritten records to sophisticated computer software packages, available for inventorying of biological agents. The use of paper-based inventory systems can be time consuming and may result in the accidental omission of samples, failure to record all necessary inventory information, and the inadvertent introduction of errors.[60] However, it is unclear whether investment in a software package for biological agent inventory reduces input errors and/or decreases the number of incidents of loss, theft, or misuse of infectious materials, or if low-tech solutions are sufficient to mitigate these risks. Therefore, there is a need for studies that compare various biological agent inventory modalities to determine their efficacy in preventing incidents.

Table 28. Notional Research Design for Efficacy of Biological Agent Inventory Modalities	
Research Goal	To generate data on the efficacy of different biological agent inventory modalities

Table 28. Notional Research Design for Efficacy of Biological Agent Inventory Modalities	
Key Variables	• Labeling scheme for inventoried items • Inventory modality (e.g., handwritten, excel spreadsheet, software package with or without barcode system, etc.) • Input fields (e.g., agent name and characteristics, source, initial quantity acquired, current quantity, storage location, etc.) • Inventory access frequency (e.g., daily, weekly, etc.) • Number of individuals who access inventory records • Number of samples and/or entries in inventory • Security breaches of lab systems or electronic records • Assessment period (e.g., six months, one year, etc.)
Example Protocol	1. Select a cohort of laboratories with large collections of biological agents in storage. Assign each laboratory to an inventory modality group (e.g., paper-based inventory, Excel-based inventory, barcode system, etc.). 2. For each laboratory, create an inventory of the biological agents in storage using the assigned modality. 3. Train laboratory personnel at each location on appropriate inventory procedures for the assigned modality. 4. Allow personnel at each location to utilize their assigned inventory modality in accordance with the typical laboratory workflow for a selected time period (e.g., six months, one year, etc.). 5. After the selected time period has passed, perform a complete audit of the inventory at each laboratory to assess for input errors and rather those errors could have resulted in losses, thefts, or misuses of inventoried items. 6. Characterize the reasons for input errors (e.g., typos, mislabeling, improper terminology, handwriting issues, etc.) and catalog any known losses or thefts. 5. Compare the outcomes for each inventory modality to determine the method that is most effective in reducing errors and/or decreasing the number of agent losses, thefts, or misuses.
Experimental Outputs	Efficacy of different biological agent inventory modalities for reducing input errors and/or decreasing the number of inventory-related incidents

3.3 Data Needs for Storage of Biological Wastes for Decontamination

3.3.1. Non-traditional packaging for containment of biological wastes

Biohazardous wastes (e.g., used culture medium, sharps, petri dishes, serological pipettes, bench papers, PPE, etc.) are often stored prior to treatment and disposal. In high-resource settings, biohazardous wastes are typically stored in specialized containers such as sealed culture flasks, sharps containers, and biohazard bags. However, these purpose-made containers may not be readily available in resource-constrained settings. There is a need for data regarding the efficacy of non-traditional packaging for containment of biohazardous waste in settings with limited resources. Studies should be conducted with different classes of biological agents or a non-biological tracer, different waste types, and a variety of potential packaging materials to identify non-traditional packaging that can safely contain a given biohazardous waste type.

Table 29. Notional Research Design for Efficacy of Non-Traditional Packaging for Containment of Biohazardous Wastes	
Research Goal	To generate data on the efficacy of non-traditional packaging for containment of biohazardous wastes

Table 29. Notional Research Design for Efficacy of Non-Traditional Packaging for Containment of Biohazardous Wastes	
Key Variables	• Biological agent/surrogate type (e.g., bacteria, virus, etc.) and concentration or non-biological tracer • Biohazardous waste type (e.g., culture medium, PPE, sharps, petri dishes, bench paper, etc.) • Packaging material (e.g., cardboard box, milk jug, conventional trash bag, bucket, etc.) • Duration of storage (e.g., days, weeks, months, etc.) • Storage conditions (e.g., location, environmental conditions, exposure to weather or other adverse conditions, etc.) • Sampling method (e.g., swab, RODAC plate, fluorescence under UV exposure, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.)
Example Protocol	1. Inoculate materials with the selected concentration of the chosen biological agent/surrogate or non-biological tracer that has been mixed/diluted to mimic actual waste materials. 2. Close container and use chosen sampling method and scheme to test for the presence of the agent or tracer on the outside of the container as a baseline. 3. Store packaged waste in selected conditions for selected duration. 4. Use selected sampling method and scheme to test for presence of the target biological agent on the outside of the container, particularly at potential weak points such as seams or closures, and in the general storage area. 5. If the non-traditional packaging effectively contains the biohazardous waste during storage, test the ability of the packaging to withstand transport to the waste treatment location and completion of the treatment process.
Experimental Outputs	Efficacy of non-traditional packaging for containment of biohazardous wastes

3.3.2. Appropriate storage conditions for biohazardous wastes

As mentioned previously, biohazardous wastes are often stored prior to treatment and disposal. In cases where wastes are stored for long periods, the conditions of storage may be important to prevent further proliferation of biological agents in the wastes. The WHO has provided some guidance regarding appropriate storage conditions for infectious waste in healthcare settings (i.e., 3-8°C if stored longer than one week); however, it is unclear what evidence this recommendation is based upon.[61] Thus, there is a need for real-world data regarding conditions which slow or prevent agent growth or other undesirable degradation (e.g., putrefaction, bloating, etc.) during storage. Experiments should be conducted with different biological agents and various waste types in a variety of storage containers.

Table 30. Notional Research Design for Appropriate Storage Conditions for Biohazardous Wastes	
Research Goal	To generate data on conditions that minimize or prevent proliferation of biological agents during storage of biohazardous wastes
Key Variables	• Biological agent type (e.g., bacteria, virus, etc.) and concentration • Biohazardous waste type (e.g., culture medium, used PPE, petri dishes, bench papers, animal tissues, etc.) • Packaging material (e.g., closed/open, insulated, etc.) • Duration of storage (e.g., days, weeks, months, etc.) • Storage conditions (e.g., ambient temperature and relative humidity) • Sampling method and scheme
Example Protocol	1. Inoculate chosen material with the selected concentration of the chosen biological agent or surrogate.

Table 30. Notional Research Design for Appropriate Storage Conditions for Biohazardous Wastes	
	2. Place in waste storage container and store in chosen environmental conditions. 3. Use sampling method and scheme to test for agent proliferation on the chosen schedule. 4. If proliferation occurs, adjust storage conditions and re-test until proliferation is minimized or prevented.
Experimental Outputs	Conditions that minimize or prevent the proliferation of a given biological in waste during storage

3.3.3. Rates of cross-contamination in mixed waste storage rooms

Laboratories often generate various types of waste (e.g., biohazardous waste, chemical waste, radiological wastes, etc.) that each have their own treatment and disposal processes. Ideally, these various waste streams are collected and stored independently so that cross-contamination is not a concern. However, small laboratories and those in resource-constrained settings may not have the space needed to segregate different waste types; instead, collecting and storing different waste types in a single small area. Therefore, there is a need for real-world data from labs that store wastes in shared areas on the rates and causes of cross-contamination from biohazardous waste to other waste types stored in the same location to inform the development of effective mitigation measures. Experiments should be carried out with different pathogen types and with different types of wastes stored in the typical packaging used in the laboratory. If cross-contamination occurs, mitigation strategies should be developed and tested to determine their effectiveness in reducing the rates of pathogen spread.

Table 31. Notional Research Design for Rates of Cross-Contamination in Mixed Waste Storage Areas	
Research Goal	To generate data on the rates and causes of cross-contamination within a mixed waste storage space and efficacy of mitigation strategies
Key Variables	• Biological agent type (e.g., bacteria, virus, etc.) and concentration or non-biological tracer • Biohazardous waste type (e.g., culture medium, used PPE, petri dishes, bench papers, etc.) • Packaging material (e.g., closed/open, insulated, etc.) • Placement of wastes within room • Duration of storage (e.g., days, weeks, months, etc.) • Sampling method and scheme • Mitigation strategies (e.g., placement of physical barriers, airflow adjustments, additional packaging, etc.)
Example Protocol	1. In a mixed-use storage space, develop sampling method and schedule appropriate for the specific facility. 2. Sample for cross-contamination between different waste types according to chosen scheme. 3. If cross-contamination occurs: a) Perform root-cause analysis to determine the cause of the cross-contamination event (e.g., splatter, human error, etc.). b) Implement chosen mitigation strategies and determine their efficacy.
Experimental Outputs	Rates and mechanisms of cross-contamination in mixed waste storage rooms; development of effective mitigation strategies to prevent cross-contamination in these settings

4. Research Opportunities Related to Cleaning

4.1 Data Needs for Cleaning

4.1.1. Frequency of cleaning and decontamination

The current edition of the *BMBL* recommends decontamination of work surfaces following routine work and after any spill of biohazardous material.[11] However, there are no recognized standards for the frequency with which other surfaces in the laboratory environment should be cleaned and/or decontaminated to reduce the risk of transmission of biological agents used in the laboratory to personnel or cross-contamination to other laboratory surfaces or materials. Therefore, there is a need for data regarding the rates of contamination of laboratory surfaces other than the typical work area (e.g., doorknobs, phones, computer keyboards, equipment keypads, sink faucets, etc.) to inform the development of effective decontamination procedures and mitigation measures to reduce the rates of contamination. Experiments should be carried out in different facility types (e.g., human clinical/diagnostic labs, animal diagnostic labs, etc.) that handle various pathogen types (e.g., bacteria, viruses, fungi, etc.). The sampling scheme used should assess for a detectable level of contamination of a variety of surfaces and should be conducted on a set schedule to determine the frequency with which contamination occurs and the causes of contamination. If contamination occurs, different chemical disinfectants and decontamination methods should be tested to develop an effective decontamination procedure for each surface.

Table 32. Notional Research Design for Rates of Contamination of Environmental Surfaces in the Laboratory

Research Goal	To generate data on the rates of contamination of environmental surfaces in the laboratory to inform the development of mitigation measures and effective decontamination procedures
Key Variables	• Facility and pathogen types • Sampling method (e.g., swabs, RODAC plates, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.) • Mitigation measure to prevent contamination (e.g., frequent glove changes, use of show covers, transport in secondary containers, etc.) • Chemical disinfectant, decontamination method (e.g., surface wipe or spray down, gas decontamination, etc.) and schedule
Example Protocol	1. Use selected sampling method and scheme to assess for contamination of environmental surfaces in the laboratory. 2. Repeat sampling on the selected schedule (e.g., daily, weekly, etc.), to determine the frequency with which contamination occurs. 3. If contamination occurs: a) Attempt to determine the cause of the contamination and implement mitigation measures intended to prevent contamination from occurring. b) Decontaminate the area using the chosen disinfectant and decontamination method to remove contamination from the surface. 4. Use sampling method and scheme to determine efficacy of the chosen mitigation measures and decontamination procedure. a) If contamination continues to occur, adjust mitigation measures and resample until contamination is minimized. b) If viable biological agent remains after decontamination, adjust parameters within the decontamination procedure and re-test until no viable agent remains.
Experimental Outputs	Rates of contamination of environmental surfaces in the laboratory; effective mitigation measures to prevent contamination; development of effective decontamination procedures

Table 32. Notional Research Design for Rates of Contamination of Environmental Surfaces in the Laboratory	
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Farnsworth CW et al. (2020) Evaluation of the risk of laboratory microbial contamination during routine testing in automated clinical chemistry and microbiology laboratories. *Clin Chem.* 66 (9)**:** 1190-1199.

4.1.2. Contamination of cleaning equipment

As mentioned above, there are no recognized standards for cleaning of surfaces in the laboratory environment that are not used for work with biohazardous materials (e.g., floors, walls, sinks, etc.). Despite this absence of standards, cleaning of these environmental surfaces is important, as failure to do so can result in laboratory contamination events.[62] Unfortunately, researchers have demonstrated that equipment used for cleaning, such as wet mops, often harbor microorganisms, and their use may spread contamination throughout the space.[63] For this reason, there is a need for data on the rates of contamination of common cleaning equipment used to clean the non-work areas within the laboratory. Experiments should be carried out in different facility types (e.g., human diagnostic labs, animal diagnostic labs, etc.) that handle various pathogen types (e.g., bacteria, viruses, fungi, etc.). If contamination of cleaning equipment occurs, decontamination methods should be tested to develop an effective decontamination procedure for each item to inform the development of effective decontamination procedures and/or mitigation strategies. Alternatively, testing could be conducted to determine if the addition of chemical disinfectants to the water used for routine cleaning can prevent buildup of contamination on cleaning equipment.

Table 33. Notional Research Design for Rates of Contamination of Cleaning Equipment	
Research Goal	To generate data on the rates of contamination of equipment utilized during routine cleaning of the laboratory to inform the development of effective mitigation and/or decontamination procedures
Key Variables	• Facility and pathogen types • Environmental surface being cleaned (e.g., floor, wall, sink, etc.) • Cleaning equipment type (e.g., broom, mop, sponge, etc.) and use frequency • Sampling method (e.g., swabs, RODAC plates, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.) • Mitigation strategies (e.g., use of disinfectant in mop water, one-time use of cleaning instrument, etc.) • Decontamination method (e.g., soak in disinfectant, autoclave, etc.), parameters (e.g., chemical concentration & exposure time, autoclave temperature and cycle length, etc.), and schedule
Example Protocol	1. Use new cleaning instrument (e.g., mop/broom head, sponge, etc.) to clean the selected surface in accordance with the typical procedure used in the laboratory. 2. After cleaning, use the chosen sampling method to assess the cleaning instrument for the presence of biological agents. 3. If contamination occurs: a) Implement chosen mitigation strategies and determine their efficacy. b) Implement select decontamination protocol and determine its efficacy.
Experimental Outputs	Rates of contamination of equipment used to clean environmental surfaces in the laboratory; development of effective decontamination procedures and/or contamination mitigation strategies for cleaning equipment

Table 33. Notional Research Design for Rates of Contamination of Cleaning Equipment	
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Ikawa JY, Rossen JS. (1999) Reducing bacteria in household sponges. *J Environ Health.* 62**:** 18-22. • Møretrø T et al. (2022) Bacterial levels and diversity in kitchen sponges and dishwashing brushes used by consumers. *J Appl Microbiol.* 133 (3)**:** 1378-1391. • Westwood JC, Mitchell MA, Legacé S. (1971) Hospital sanitation: the massive bacterial contamination of the wet mop. *Appl Microbiol.* 21 (4)**:** 693-697.

4.2. Data Needs for Cleaning Gross Contamination

4.2.1. Selection of PPE for use during cleaning of gross contamination from surfaces

In laboratories, PPE is used in combination with engineering controls to protect personnel from exposure to biological agents. PPE selection is typically based on the biological agents in use and the procedures being conducted.[64] However, the same PPE set worn during research procedures may not be adequate for use during cleaning due to different contamination risks (e.g., liquid splashes, aerosols, airborne particles, etc.), necessitating a separate risk assessment of required PPE. There is a need for data regarding the rates of contamination of research personnel during cleaning of gross contamination containing biological agents to inform the selection and use of appropriate PPE. Studies should be conducted with different types of gross contamination, a variety of cleaning methods, and multiple pathogen types.

Table 34. Notional Research Design for Selection of PPE During Cleaning of Gross Contamination	
Research Goal	To generate data on the rates and types of contamination in air or retained on the clothing and/or body of personnel during cleaning of gross contamination containing biological agents
Key Variables	• Biological agent/surrogate type (e.g., virus, bacteria, fungus, etc.) and concentration or non-biological tracer • Gross contamination type (e.g., wet/dry, animal feces, soil, blood, etc.) and amount • Cleaning method (e.g., physical removal methods, heat treatments, etc.) • Sampling methods for various test samples (e.g., hair, skin, clothing, air, etc.) • PPE use procedures (e.g., PPE types needed, donning & doffing procedures, etc.) • Training and experience of personnel conducting cleaning procedure
Example Protocol	1. Simulate common types of gross contamination spiked with biological agent/surrogate or non-biological tracer and have personnel clean up the contamination using the selected cleaning method. 2. Sample personnel and air for contamination during and after cleaning of gross contamination. 3. Evaluate frequency, amount, and location of contamination for a given contamination type and cleaning method combination. 4. Develop appropriate PPE use procedures. 5. Test for reduction in the rates of personnel contamination due to modified PPE use.
Experimental Outputs	Rates and types of contamination retained on the clothing and body of personnel during cleaning of gross contamination; development of appropriate PPE use procedures

Table 34. Notional Research Design for Selection of PPE During Cleaning of Gross Contamination	
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Bell T et al. (2015) Ebola virus disease: The use of fluorescents as markers of contamination for personal protective equipment. *IDCases.* 2 (1)**:** 27-30. • Hall S et al. (2018) Use of ultraviolet-fluorescence-based simulation in evaluation of personal protective equipment worn for first assessment and care of a patient with suspected high-consequence infectious disease. *J Hosp Infect.* 99 (2)**:** 218-228.

4.2.2. Efficacy of cleaning methods on various types of gross contamination

Current editions of the *BMBL* and the *LBM* both recommend pre-cleaning of soiled items and surfaces prior to decontamination. A variety of manual methods, which may be supplemented with heat treatment, are available for removal of gross contamination; however, guidelines that indicate appropriate methods for cleaning a specific contamination type associated with a given material or surface are not available.[11,12] As such, there is a need for data to inform selection of an appropriate cleaning method for each contamination type and item/surface combination.

Table 35. Notional Research Design for Efficacy off Cleaning Methods for Gross Contamination	
Research Goal	To generate data on the efficacy of various methods for removing gross contamination prior to chemical disinfection
Key Variables	• Gross contamination type (e.g., wet/dry, animal feces, soil, blood, etc.) and amount • Cleaning method (e.g., scraping, scrubbing, wiping, pressure washing, etc.) • Heat treatment (e.g., steam, hot water spray, etc.) • Item (e.g., animal caging, boots, instruments, etc.) or surface (e.g., flooring, counter tops, stainless steel sink, etc.) • Training and experience of personnel conducting cleaning procedure • Sampling and testing methods (e.g., ATP testing, microscopic inspection, contact angle measurement, wettability measurement, etc.)
Example Protocol	1. Generate gross contamination on the selected item or surface. 2. Clean gross contamination using the chosen method. 3. Use chosen sampling method to test for the presence of remaining contamination or residue after cleaning.
Experimental Outputs	Development of effective procedures for complete removal of organic material from a specific type of gross contamination associated with a specific surface/material type
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Birch W, Carré A, Mittal KL. (2008) Chapter 13 - Wettability Techniques to Monitor the Cleanliness of Surfaces. In *Developments in Surface Contamination and Cleaning*. Kohli R, Mittal KL (eds.). 693-723. Norwich, NY: William Andrew Publishing. • Merritt K, Hitchins VM, Brown SA. (2000) Safety and cleaning of medical materials and devices. *J Biomed Mater Res*. 53 (2): 131-136. • Nelson SW et al. (2023) Efficacy of detergent-based cleaning and wiping against SARS-CoV-2 on high-touch surfaces. *Lett Appl Microbiol*. 76 (3).

4.2.3. Surface decontamination without pre-cleaning

Both the *LBM* and the *BMBL* recommend that pre-cleaning procedures be used to physically remove dirt or other organic substances from items and surfaces prior to decontamination as the presence of

these substances may interfere with the activity of chemical disinfectants.[11,12] However, there may be instances when it is desirable to decontaminate prior to cleaning due to the increased hazards (e.g., creation of infectious aerosols, splashes, etc.) that cleaning procedures may present. Thus, there is a need for development of protocols for effective decontamination of surfaces with high organic loads in the absence of pre-cleaning.

Table 36. Notional Research Design for Surface Decontamination without Pre-Cleaning

Research Goal	To generate data on the decontamination of surfaces with high organic loads without pre-cleaning
Key Variables	• Target biological agent and concentration • Gross contamination type (e.g., wet/dry, animal feces, soil, blood, etc.) and amount • Decontamination method (e.g., chemical, heat treatment, UV light, etc.) and parameters (e.g., chemical concentration, exposure/contact time, etc.) • Surface type • Sampling (e.g., RODAC plates, swabs, etc.) and testing methods
Example Protocol	1. Inoculate selected organic material and surface with a known concentration of the target organism. 2. Expose the contaminated surface to the selected decontamination protocol. 3. Attempt to recover the target organism to determine decontamination method and parameters that effectively kill the target organism in the presence of organic material.
Experimental Outputs	Protocol for decontamination of surface with high organic loads without pre-cleaning
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Krug PW et al. (2018) Disinfection of transboundary animal disease viruses on surfaces used in pork packing plants. *Vet Microbiol.* 219**:** 219-225. • Nerandzic MM et al. (2012) Evaluation of a hand-held far-ultraviolet radiation device for decontamination of Clostridium difficile and other healthcare-associated pathogens. *BMC Infect Dis.* 12**:** 120. • Pottage T et al. (2010) Evaluation of hydrogen peroxide gaseous disinfection systems to decontaminate viruses. *J Hosp Infect.* 74 (1)**:** 55-61.

5. Research Opportunities Related to Decontamination

5.1 Data Needs for Development and Testing of Decontamination Protocols

5.1.1. Evaluation of neutralizers for chemical disinfectants

Chemical decontamination protocols are often validated using viability testing whereby the material is tested for remaining viable microbes that indicate decontamination failure; however, the presence of residual chemical decontaminant may interfere with viability testing.[65] For this reason, chemical decontaminants must be shown not to interfere with viability testing or be neutralized before the testing is conducted.[66] Dey-Engley (D/E) neutralizing broth and Letheen broth are commonly used for this purpose, but their neutralizing ability has not been tested for all chemical disinfectants.[66,67] So, there is a need for data regarding the ability of these media, or other potential neutralizers, to neutralize chemical disinfectants for which this testing has not already been completed. Each neutralizer should be evaluated for both its efficacy in neutralizing the target disinfectant and its non-toxicity toward the target pathogen.[65]

Table 37. Notional Research Design for Evaluation of Neutralizers for Chemical Disinfectants	
Research Goal	To generate data on the ability of neutralizing media to inactivate chemical disinfectants while allowing survival of biological agents
Key Variables	• Biological agent type (e.g., bacteria, virus, mammalian cells, etc.) and concentration • Chemical disinfectant type (e.g., alcohol-based, quaternary ammonium compound, etc.), concentration, and exposure time • Neutralizer
Example Protocol	1. To evaluate the efficacy of Letheen broth as a neutralizer for a specific chemical disinfectant used to decontaminate samples containing a bacterial pathogen, begin by preparing two fresh broth cultures containing a known concentration of the microbe. 2. Expose the bacterial population in the first tube to a volume of the chemical disinfectant, without Letheen broth, for 30 minutes (biocide only). 3. Expose the bacterial population in the second tube to equal volumes of the chemical disinfectant and Letheen broth for the appropriate exposure time (biocide + neutralizer). 4. Recover surviving bacteria from each treatment by plating on an appropriate agar medium. The presence of viable agent in the biocide + neutralizer treatment and not in the biocide only treatment indicates that the bacterium is susceptible to the chemical disinfectant and that Letheen broth is a suitable neutralizer for the chemical disinfectant. 5. To evaluate Letheen broth toxicity toward the bacterial pathogen, use the microbe to inoculate a tube containing standard growth broth (viability control) and another tube containing only Letheen broth (neutralizer only) and incubate for 30 minutes. 6. Recover surviving bacteria from each treatment by plating on an appropriate agar medium. The presence of viable agent at similar concentrations indicates that the neutralizing broth is not toxic to the bacteria pathogen.
Experimental Outputs	Effective neutralizer for use in validation of a decontamination protocol using a specific chemical disinfectant with a specific target pathogen
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Dey BP, Engley FB, Jr. (1995) Comparison of Dey and Engley (D/E) Neutralizing Medium to Letheen Medium and Standard Methods Medium for recovery of Staphylococcus aureus from sanitized surfaces. *J Ind Microbiol.* 14 (1)**:** 21-25. • Eissa ME et al. (2012) Neutralizer evaluation study of some microbial isolates against two strong disinfectants with and without the presence of synthetic detergent. *World Appl Sci J*. 20 (6): 823-831. • Johnston MD et al. (2002) A rapid method for assessing the suitability of quenching agents for individual biocides as well as combinations. *J Appl Microbiol.* 92 (4)**:** 784-789.

5.1.2. Standardized testing and reporting methodology for decontamination protocols

Many laboratories develop and test decontamination protocols for the biological agents and materials they work with as part of their overarching research programs. These protocols are not generally included in publications reporting the results of experimental studies and when they are, the details of how the protocols were developed and validated are often absent. Due to this lack of detail, other laboratories that wish to use the protocol must undertake additional experimentation to optimize and validate the protocol. For this reason, standardization of a testing and reporting methodology for decontamination protocols is needed to facilitate sharing of these protocols among labs worldwide and to streamline the in-house validation process.

Table 38. Notional Research Design for Standardization of Testing and Reporting Methodologies for Decontamination Protocols	
Research Goal	To develop a standardized testing and reporting methodology for decontamination protocols
Key Variables	• Biological agent type (e.g., bacteria, virus, etc.) and concentration • Decontamination method and use parameters (e.g., chemical concentration and exposure time, UV wavelength and exposure time, etc.) • Reagents and equipment used • Step-by-step procedure
Example Protocol	1. Analyze published and unpublished decontamination protocols from a variety of labs to identify necessary data elements (e.g., materials & equipment used, protocol steps, laboratory techniques, workflows, etc.). 2. Use analysis to establish common terminology, data elements, and procedure descriptions for reporting. 3. Develop common reporting method or model report for sharing of protocols. 4. Share method with broad stakeholder group for feedback and movement toward consensus of new standard. 5. Iterate as needed to develop consensus.
Experimental Outputs	Standardized testing and reporting method for decontamination protocols
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Giraldo O, Garcia A, Corcho O. (2018) A guideline for reporting experimental protocols in life sciences. *PeerJ.* 6**:** e4795.

5.2 Data Needs for Chemical Decontamination

5.2.1. Efficacy of chemical disinfectants beyond the manufacturer's expiration date

Chemical disinfectants are typically labeled with an expiration date that the manufacturer determines by conducting real-time or accelerated aging studies that assess the degradation of the product's active ingredients and/or efficacy over time.[68,69] However, it is unclear whether disinfectants may remain effective beyond the expiration date when stored in optimal conditions as listed on the product label or other documentation (i.e., a safety data sheet or similar document). Thus, there is a need for real-world data regarding how long chemical disinfectants and/or their active component(s) retain their efficacy under optimal storage conditions. Such data will support safe use of these disinfectants in facilities where pathogenic organisms are handled and may provide justification for use beyond the manufacturer's expiration date in resource constrained settings. Studies related to this data need should include various biological agent types (e.g., bacteria, viruses, fungi, spores, prions, etc.) and a variety of relevant chemical disinfectants (e.g., alcohols, chlorine compounds, peroxides, phenolics, quaternary ammonium compounds, etc.). Additional studies that assess other parameters related to the efficacy of chemical disinfectants (e.g., storage at inappropriate temperatures, exposure to light, etc.) may be needed to further support the use of chemical disinfectants in under-resourced settings.

Table 39. Notional Research Design for Efficacy of Chemical Disinfectants Beyond the Expiration Date	
Research Goal	To generate data on the efficacy of chemical disinfectants and/or their active component(s) beyond the manufacturer's expiration date

Table 39. Notional Research Design for Efficacy of Chemical Disinfectants Beyond the Expiration Date	
Key Variables	• Biological agent type and concentration • Chemical disinfectant/active component(s) • Number of replicates/number of bottles • Method for testing efficacy (e.g., American Society for Testing and Materials [ASTM] E2197, EN 12469, EN 13610, EN 13697, EN 1276, EN 16437, Environmental Protection Agency [EPA] Office of Chemical Safety and Pollution Prevention [OCSPP] 810:2100, etc.) • Testing timeline (e.g., monthly, every three months, etc.)
Example Protocol	1. Select a chemical disinfectant or active component for testing and procure multiple containers from a single manufacturer or chemical supplier. 2. When the containers are received, use the selected method to test the efficacy of each against the selected biological agent(s). Retain efficacy data for later use. 3. Store the containers in accordance with the manufacturer recommendations, as listed on the product label and/or other associated documentation, until the expiration date is reached. 4. On the expiration date, use the selected method to test the efficacy of the disinfectant in each container against the select biological agent(s) as in Step 2 above. 5. Compare the efficacy of the disinfectant/component in each container on the expiration date to the data retained from the initial testing. 6. If there is no significant reduction in efficacy, continue storing the containers and re-testing on the selected testing timeline until the efficacy is significantly reduced. 7. If the disinfectant remains effective beyond the listed expiration date, repeat testing with disinfectant from additional manufacturers/suppliers to determine if similar results can be obtained.
Experimental Outputs	Evidence-based recommendation for continued use of chemical disinfectants beyond the manufacturer's expiration date
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • ASTM International. (2024) ASTM E2197: Standard Quantitative Disk Carrier Test Method for Determining Bactericidal, Virucidal, Fungicidal, Mycobactericidal, and Sporicidal Activities of Chemicals. West Conshohocken, PA, USA: ASTM International. • British Standards Institute. (2000) BS EN 12469: Biotechnology - Performance Criteria for Microbiological Safety Cabinets. London, England: British Standards Institute. • British Standards Institute. (2002) BS EN 13610: Chemical disinfectants - Quantitative suspension test for the evaluation of virucidal activity against bacteriophages of chemical disinfectants used in food and industrial areas. London, England: British Standards Institute. • British Standards Institute. (2015) BS EN 13697: Quantitative Non-porous Surface Test for the Evaluation of Bactericidal and/or Fungicidal Activity of Chemical Disinfectants Used in Food, Industrial, Domestic and Institutional Areas. London, England: British Standards Institute. • British Standards Institute. (2019) BS EN 1276: Chemical Disinfectants and Antiseptics - Quantitative Suspension Test for the Evaluation of Bactericidal Activity of Chemical Disinfectants and Antiseptics Used in Food, Industrial, Domestic and Institutional Areas. London, England: British Standards Institute. • British Standards Institute. (2019) BS EN 16437: Chemical Disinfectants and Antiseptics - Quantitative Surface Test for the Evaluation of Bactericidal Activity of Chemical Disinfectants and Antiseptics Used in Veterinary Area on Porous Surfaces Without Mechanical Action. London, England: British Standards Institute. • Office of Chemical Safety and Pollution Prevention. (2018) EPA Product Performance Test Guidelines - OCSPP 810.2100: Sterilants, Sporicides, and Decontaminants. Washinton, DC, USA: U.S. Environmental Protection Agency. Available from: https://www.regulations.gov/document/EPA-HQ-OPPT-2009-0150-0035.

5.2.2. Chemical disinfectant compatibility with various laboratory surface types

Current editions of the *BMBL* and the *LBM* recommend routine decontamination of laboratory surfaces and equipment used with biological agents or other biohazardous materials.[11,12] It is known that some chemical disinfectants, such as bleach, should not be used for decontamination of stainless steel surfaces in laboratory equipment because they are corrosive and may damage the surfaces over time.[70-72] However, researchers are not always aware of surface compatibility information for other chemical disinfectants. Some disinfectant manufacturers provide this compatibility information for their products and laboratory studies have assessed the compatibility of disinfectants with different surface types, but there is no single resource that laboratory personnel can use to determine which disinfectants are compatible with the various surfaces in their laboratories.[73,74] As such, there is a need for development of a compatibility matrix that delineates the chemical disinfectants that can be used to decontaminate various laboratory surfaces (e.g., walls, floors, cabinets, etc.) without corrosive effects. This study will involve a comprehensive review of the scientific literature and cataloging of the compatibility information available from disinfectant manufacturers to determine those combinations that have already been tested. For those combinations for which compatibility information is not already available, laboratory studies can then be carried out to test the effects that a given disinfectant has on various surface types.

Table 40. Notional Research Design for Compatibility of Chemical Disinfectants with Laboratory Surfaces

Research Goal	To assess the compatibility of chemical disinfectants with various laboratory surfaces to inform the development of a chemical disinfectant-surface compatibility matrix
Key Variables	• Surface material (e.g., various metals & alloys, glass, plastics & polymers, phenolic or epoxy resin, etc.) • Chemical disinfectant and use parameters (e.g., chemical concentration, contact time, inclusion of water rinse, etc.) • Environmental conditions during use (e.g., temperature, relative humidity, etc.) • Treatment frequency (e.g., daily, weekly, etc.) • Method for characterizing surface degradation or corrosion (e.g., optical microscopy, contact angle, atomic force microscopy, weight etc.) [75]
Example Protocol	1. Expose the test surface to the chemical disinfectant using the selected parameters. 2. After treatment, assess surface for degradation/corrosion caused by the disinfectant. 3. Repeat process regularly over the course of the study to determine what, if any, degradative impacts can be associated with continued use of the disinfectant over time.
Experimental Outputs	Compatibility of chemical disinfectants with various laboratory surfaces; Chemical disinfectant-surface compatibility matrix resource
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Abban S, Jakobsen M, Jespersen L. (2013) A practical evaluation of detergent and disinfectant solutions on cargo container surfaces for bacteria inactivation efficacy and effect on material corrosion. *Afr J Biotechnol.* 12 (23)**:** 3689-3698. • LANXESS. (2022) Virkon S - Vehicle Disinfection Materials Compatibility. Prepared for LANXESS Corporation. https://www.qcsupply.com/media/product_attachments/attachment_file/v/i/virkon_s_vehicle_disinfectant_compatibility.pdf. • Teska P et al. Characteristics of an Ideal Surface Damage Testing Protocol. https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Archived:

Table 40. Notional Research Design for Compatibility of Chemical Disinfectants with Laboratory Surfaces	
	https://web.archive.org/web/20240208164254/https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Accessed February 7, 2024. • Verran J, Boyd RD. (2001) The relationship between substratum surface roughness and microbiological and organic soiling: A review. *Biofouling.* 17 (1)**:** 59-71.

5.2.3. Testing disinfectants on different presentations of biological agents

Manufacturers of chemical disinfectants test efficacy against only a limited set of typical pathogen presentations based on the intended use of the product. However, it is unclear if disinfectants, used as labeled, are effective against non-typical presentations of a given pathogen (e.g., dried aerosol, organism dried in a thick layer, high concentration, frozen culture, etc.). As such, there is a need for empirical data regarding the efficacy of a disinfectant, labeled for activity against a given pathogen, against non-typical presentations of that pathogen.

Table 41. Notional Research Design for Disinfectant Efficacy Against Non-Typical Presentations of Biological Agents	
Research Goal	To generate data on the efficacy of disinfectants against non-typical presentations of pathogens
Key Variables	• Biological agent type (e.g., bacteria, virus, etc.), presentation, and concentration • Chemical disinfectant and use parameters (e.g., chemical concentration and contact time, temperature, etc.) • Testing method and scheme (e.g., quantitative suspension test, carrier test, quantitative non-porous surface test, in-place viability test, etc.) [76,77]
Example Protocol	1. To perform a quantitative non-porous surface test, inoculate non-porous surface with a known concentration of the selected presentation of the target biological agent. 2. Apply disinfectant at the appropriate concentration for the manufacturer recommended exposure time. 3. Apply neutralizing solution. 4. Serially dilute neutralizing solution and plate to recover surviving biological agent. 5. If viable agent is recovered, alter parameters (e.g., increased disinfectant concentration and/or exposure time) and repeat protocol to determine efficacy against the given agent presentation.
Experimental Outputs	Efficacy of disinfectants on non-typical presentations of biological agents for use in development of effective decontamination protocols
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Guan J et al. (2013) Influence of temperature and organic load on chemical disinfection of Geobacillus steareothermophilus spores, a surrogate for Bacillus anthracis. *Can J Vet Res*. 77 (2): 100-104. • Holah JT et al. (1998) Future techniques for disinfectant efficacy testing. *Int Biodeterior Biodegrad.* 41**:** 273-279. • Sattar SA et al. (2003) A disc-based quantitative carrier test method to assess the virucidal activity of chemical germicides. *J Virol Methods.* 112 (1)**:** 3-12. • Skowron K et al. (2019) Disinfectant susceptibility of biofilm formed by Listeria monocytogenes under selected environmental conditions. *Microorganisms*. 7 (9). • Tarka P, Nitsch-Osuch A. (2021) Evaluating the virucidal activity of disinfectants according to European Union standards. *Viruses.* 13 (4). • van Klingeren B et al. (1998) Assessment of the efficacy of disinfectants on surfaces. *Int Biodeterior Biodegrad.* 41 (3)**:** 289-296.

5.2.4. Treatment of waste from cleanup of biological spills

The most used method for cleanup of biological spills involves covering the spill with paper towels or another absorbent material, saturating the spill and absorbent material with an effective disinfectant and allowing to set for the indicated contact time, then collecting the absorbent material and treating as biohazardous waste (i.e., placed in biohazard bags and decontaminated via autoclaving or incineration)[39,40]. However, there is a lack of empirical evidence to indicate that these materials are harboring residual biological agents, and that additional decontamination is warranted. These data will ensure that resources are not wasted treating wastes that no longer contain infectious organisms. Experiments should be carried out with various pathogen types (e.g., bacteria, viruses, fungi, etc.) and properties (e.g., enveloped & non-enveloped viruses, Gram-positive & -negative bacteria, etc.), different absorbent materials (e.g., paper towels, commercial spill pads, spill socks/pillows, vermiculite, etc.) and a variety of disinfectants shown to be effective against the selected agents.

Table 42. Notional Research Design for Treatment of Waste from Cleanup of Biological Spills

Research Goal	To generate data on the rates of residual infectious organisms present on absorbent material after spill cleanup procedures involving chemical disinfectants
Key Variables	• Spill parameters (e.g., biological agent type and concentration, liquid type, spill volume, etc.) • Absorbent material • Chemical disinfectant and contact time • Sampling method and scheme
Example Protocol	1. Create a biological spill with the selected parameters. 2. Use disinfectant to clean up the spill in accordance with the SOP used in the laboratory being sure to allow for the appropriate contact time recommended by the manufacturer of the disinfectant. 3. Collect used absorbent material and sample for the presence of residual infectious organisms.
Experimental Outputs	Rates of presence of infectious organisms present on absorbent material after spill cleanup procedures; evidence-based treatment and disposal procedures for waste generated to cleanup of biological spills
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Idu EG, Nwaubani D. (2019) Isolation, characterization and identification of bacteria emanating from sawdust generated in Ahiake sawmill, Umuahia, Abia State, Nigeria. *Int J Res Sci Eng*. 10 (6): 1547-1555. • Robinton ED, Mood EW. (1968) A study of bacterial contaminants of cloth and paper towels. *Am J Public Health Nations Health*. 58 (8): 1452-1459.

5.2.5. Efficacy of chemical decontamination of liquid biological wastes

Chemical disinfectants are commonly used to decontaminate liquid biological wastes; however, the efficacy of this process is often questioned because disinfectants are approved only for use on non-porous surfaces.[12,78] Additionally, the discovery of genetically modified organisms in wastewater indicates that failure of protocols for the chemical inactivation of liquid wastes may result in the release of agents from laboratory settings.[79,80] Thus, there is a need for the development and validation of evidence-based methods for the decontamination of liquid samples using chemical disinfectants. Studies should be conducted with a variety of sample matrices, biological agents, and chemical disinfectants.

Table 43. Notional Research Design for Chemical Decontamination of Liquid Biohazardous Wastes	
Research Goal	To generate data on the efficacy of decontamination of liquid biohazardous wastes with chemical disinfectants
Key Variables	• Biological agent type (e.g., bacteria, virus, fungi, etc.), properties (e.g., presence of viral envelope, bacterial Gram reaction, etc.) and concentration • Chemical disinfectant and use parameters (e.g., chemical concentration, contact time, age/freshness of disinfectant solution, etc.) • Sample matrix (e.g., broth medium, biological fluids, etc.) and presence of organic material that may inhibit disinfectant activity • Neutralizer for chemical disinfectant • Method for recovery of target biological agent(s)
Example Protocol	1. Select a variety of common protocols used to decontaminate liquid biohazardous wastes with chemical disinfectants. 2. Carry out each procedure using different presentations of the target agent (e.g., different sample matrices, different waste volumes, presence of organic material, etc.) and/or modification to the protocol parameters (e.g., chemical concentration, longer/shorter contact time, age of disinfectant, etc.). Neutralize chemical disinfectant and attempt to recover target biological agent from treated sample. 3. If viable agent is recovered, alter protocol parameters (e.g., different disinfectant, increased disinfectant concentration, increased exposure time, etc.) and repeat protocol until no viable agent is recovered. 4. Use data to develop evidence-based methods for the efficient and effective decontamination of liquid biohazardous wastes using chemical disinfectants.
Experimental Outputs	Efficacy of decontamination of liquid biological wastes with chemical disinfectants; development and validation of evidence-based methods for the decontamination of liquid samples using chemical disinfectants
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Chitnis V et al. (2003) Treatment of discarded blood units: disinfection with hypochlorite/formalin versus steam sterilization. *Indian J Med Microbiol.* 21 (4)**:** 265-267. • Teuscher AC et al. (2024) Effectiveness of chemical inactivation of infectious liquid biological waste: A randomized sample study of research laboratories in Switzerland. *J Biosaf and Biosecur.* 6 (1)**:** 16-26.

5.2.6. Efficacy of chemical decontamination of positive pressure protective suits worn in maximum containment laboratories

Personnel working in (A)BSL-4 suit laboratories are protected from biological hazards by wearing positive pressure suits that are decontaminated via chemical shower before exiting the laboratory.[11,12] Researchers have conducted limited studies to assess the efficacy of the chemical shower for decontamination of positive pressure suits; however, there is a need for additional research to inform the development of evidence-based decontamination protocols in various settings and conditions.[81,82] Experiments should be carried out with various pathogen types (e.g., bacteria, viruses, fungi, etc.) and properties (e.g., enveloped & non-enveloped viruses, Gram-positive & -negative bacteria, etc.), suits constructed of various materials (e.g., polyethylene, coated polyester, coated polyamide, etc.), different shower systems, assorted disinfectants, and varied procedural elements (e.g., use of scrub brush, distance from the shower nozzle, shower length, etc.).

Table 44. Notional Research Design for Efficacy of Chemical Decontamination of Positive Pressure Suits	
Research Goal	To generate data on the efficacy of chemical decontamination of positive pressure suits
Key Variables	• Biological agent type, properties, and presentation (e.g., wet, dry, in sample with high organic load, etc.) • Location of biological material on the suit • Suit material • Shower system • Chemical disinfectant and concentration • Shower parameters • Sampling method and scheme
Example Protocol	1. Contaminate the positive pressure suit with the selected pathogen or surrogate organism in the chosen concentration and form. 2. Expose the inoculated suits to the chemical shower using the selected disinfectant and procedural parameters. 3. After completion of the shower, use the chosen sampling method and scheme to recover any surviving microorganisms. 5. If viable biological agent remains, adjust chemical disinfectant and/or shower parameters and re-test until no viable agent is detected after completion the chemical shower procedure.
Experimental Outputs	Efficacy of chemical showers for decontamination of positive pressure suits; development of effective shower procedures for chemical decontamination of positive pressure suits
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Klaponski N et al. (2011) A study of the effectiveness of the containment level-4 (CL-4) chemical shower in decontaminating Dover positive-pressure suits. *Appl Biosaf.* 16 (2)**:** 112-117. • Parks SR et al. (2013) Showering BSL-4 suits to remove biological contamination. *Appl Biosaf.* 18**:** 162 - 171.

5.2.7. Efficacy of decontamination inside laboratory equipment

The current editions of both the *LBM* and *BMBL* prescribe decontamination of laboratory equipment on a routine basis and after any potential contamination event.[11,12] It is relatively easy to sample the outer, accessible portions of lab equipment for microbial contamination and disinfect these areas; however, testing and disinfection of the internal portions of equipment that could come into contact with samples or users during routine use may be more difficult. Additional consideration should be given to decontaminating internal components that may become exposed during maintenance/repair or if a piece of equipment is ever to be removed from the containment space for any reason. Real-world data regarding the frequency and causes of contamination of the internal components of different types of lab equipment are needed to inform the development of effective mitigation strategies to reduce contamination and effective decontamination procedures.

Table 45. Notional Research Design for Rates and Causes of Contamination Inside Pieces of Laboratory Equipment	
Research Goal	To generate data on the microbial contamination of internal portions of laboratory equipment for use in development of best practices for reduction of contamination and equipment disinfection
Key Variables	• Equipment type • Equipment use parameters (e.g., speed, time, frequency of use, etc.) • Biological agents used with equipment • Sampling scheme • Mitigation strategies (e.g., placement of physical barriers, use of locking tubes, etc.)

Table 45. Notional Research Design for Rates and Causes of Contamination Inside Pieces of Laboratory Equipment	
	• Chemical disinfectant • Decontamination method and frequency
Example Protocol	1. Develop an appropriate sampling scheme and use to assess for the presence of microbial contamination on internal portions of chosen equipment. 2. Determine the efficacy of chosen mitigation strategies in preventing contamination. 3. Decontaminate the area using the chosen disinfectant and method. 4. Use previously developed sampling scheme to determine the efficacy of the chose disinfectant and decontamination method.
Experimental Outputs	Rates and causes of contamination of accessible internal portions of laboratory equipment; development of effective mitigation strategies and decontamination procedures

5.2.8. Frequency of decontamination of laboratory equipment

Current editions of the *BMBL* and the *LBM* both recommend that laboratory equipment be decontaminated on a regular basis, after any spills or splashes of biohazardous material, and prior to maintenance or removal from the laboratory.[11,12] However, there are no guidelines regarding how often regular decontamination should occur. Thus, there is a need for real-world data regarding how often different pieces of equipment become contaminated during routine use. A risk-based approach to this question demands we test a variety of conditions so that data are available to fill site-specific risk assessments on this frequency.

Table 46. Notional Research Design for Frequency of Laboratory Equipment Decontamination	
Research Goal	To generate data on rates of contamination of laboratory equipment during routine use to inform the required frequency of decontamination
Key Variables	• Equipment type (e.g., centrifuge, incubator, cell sorter, etc.) and use frequency • Biological agent type and concentration used with equipment • Sampling method (e.g., swabs, RODAC plates, etc.) and scheme (e.g., sampling schedule, location of sampling, number of samples, etc.)
Example Protocol	1. Use an effective disinfectant to thoroughly decontaminate the piece of equipment. 2. Use equipment in accordance with typical laboratory workflow. 3. On selected schedule (e.g., daily, weekly, etc.), sample equipment and test for the presence of viable biological agent. Validate the decontamination method by repeating a sufficient number of times.
Experimental Outputs	Rates of contamination of laboratory equipment; evidence-based decontamination frequency for laboratory equipment
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Yarbrough Melanie L et al. (2018) Frequency of instrument, environment, and laboratory technologist contamination during routine diagnostic testing of infectious specimens. *J Clin Microbiol*. 56 (6): 10.1128/jcm.00225-00218.

5.2.9. Efficacy of chemical decontamination of organic materials

Chemical decontamination of many materials associated with research studies (e.g., soil, animal wastes, blood, plant debris, water, etc.) can be difficult because the presence of organic matter may

interfere with the activity of the chemical disinfectant or serve as a physical barrier that protects microbes in the material from coming into contact with the chemical.[83] There is a need for the development and validation of evidence-based methods for the decontamination of samples with high organic loads. Studies should be conducted with a variety of materials relevant to research and with viral, bacterial, and fungal pathogens to account for any impacts the sample or pathogen type may have.

Table 47. Notional Research Design for Decontamination of Organic Materials	
Research Goal	To generate data on the decontamination of materials with high organic loads
Key Variables	• Target pathogen • Sample to be decontaminated (e.g., animal feces, plant material, soil, water, blood etc.) • Chemical disinfectant • Disinfection parameters (e.g., application method, contact time, chemical concentration, etc.)
Example Protocol	1. Inoculate the chosen organic material with a known concentration of the target pathogen. 2. Exposed the inoculated material to the chosen disinfectant at various concentrations and exposure times. 3. Attempt to recover the target organism to determine disinfectant concentration and time that effectively kills the target organism in the organic material. 4. Validate the decontamination method by repeating a sufficient number of times.
Experimental Outputs	Validated procedure for decontamination of organic materials involved in research studies

5.2.10. Efficacy of decontamination of fomites in the field

Vehicles, tools, and equipment utilized during field studies involving biological agents may serve as fomites that can transmit the agents between sampling sites and/or to geographic areas not related to the research.[20] These experiments will involve the development of effective decontamination procedures for these items and the testing of their effectiveness. Care must be taken to ensure that the chosen disinfectant is compatible with the tested equipment and will not cause degradation such as rusting.

Table 48. Notional Research Design for Decontamination of Fomites	
Research Goal	To generate data on the decontamination of items that may serve as fomites
Key Variables	• Target biological agent and concentration • Fomite type (e.g., vehicle tires, metal tools, shoes, PPE, etc.) • Sampling scheme • Chemical disinfectant • Disinfection parameters (e.g., application method, contact time, chemical concentration, etc.)
Example Protocol	1. Inoculate potential fomites utilized in field research studies with the chosen biological agent. 2. Expose the fomite to the chosen disinfectant at various concentrations and exposure times. 3. Attempt to recover the target organism to determine disinfectant concentration and time that effectively kills the target organism. 4. Validate the decontamination method by repeating a sufficient number of times.
Experimental Outputs	Rates of contamination of potential fomites; validated decontamination method for fomites

5.3. Data Needs for Non-Chemical Decontamination

5.3.1. Efficacy of UV radiation for inactivation of various pathogens

Ultraviolet radiation has been used to inactivate pathogens on surfaces, and in air and water, since the 1980's, with UVC radiation (i.e., wavelength 200-280 nm) having the highest germicidal activity.[84-86] The technology is effective against a variety of microbes, including bacteria, viruses, and protozoa; however, validated protocols for UV inactivation of specific pathogens, particularly for use in laboratory settings, are lacking.[84,87-89] As such, there is a need for data regarding UVC inactivation of a variety of pathogen types (e.g., bacteria, virus, fungus, etc.) and properties (e.g., enveloped & non-enveloped viruses, Gram-positive & -negative bacteria, etc.), in different presentations (e.g., vegetative cells, spores, etc.) and matrices (e.g., dried, in liquid suspension, etc.), to inform the development and validation of protocols for routine decontamination of laboratory surfaces and other materials using UVC. Similar studies should be conducted to determine the efficacy and applicability of other non-chemical methods for decontamination (e.g., cold plasma, ozone, pulsed light, etc.).

Table 49. Notional Research Design for UV Inactivation of Pathogens

Research Goal	To generate data on the efficacy of UV radiation for inactivation of various pathogens
Key Variables	• Biological agent type, presentation, matrix, and concentration • Contaminated surface or material • UV wavelength (e.g., 200-280 nm) and use parameters (e.g., radiation dose/irradiance, contact time, distance to surface/material, location in the room, etc.) • UV bulb age • Ambient conditions (e.g., temperature, relative humidity, etc.) • Sampling method and scheme
Example Protocol	1. Inoculate surface/material with a known concentration of the chosen pathogen in the selected presentation. 2. Expose the inoculated surface/material to UV radiation using the selected parameters. 3. After treatment, use the chosen sampling method and scheme to recover any surviving microorganisms. 4. If surviving microbes are present, adjust UV treatment parameters and re-test until no survivors are recovered after treatment.
Experimental Outputs	Efficacy of UV radiation for inactivation of various pathogens to inform development and validation of agent- and material-specific decontamination protocols using UV radiation
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Soh TK et al. (2023) A validated protocol to UV-inactivate SARS-CoV-2 and herpesvirus-infected cells. *PLoS ONE.* 18 (5)**:** e0274065.

5.3.2. Efficacy and validation of antimicrobial surfaces

Antimicrobial surfaces, which display broad spectrum biocidal activity or prevent adherence of microorganisms, have been developed for use in a variety of areas including healthcare, textiles, and food production.[90-93] In recent years, manufacturers have developed antimicrobial surfaces for use as countertops in healthcare settings and home kitchens.[94,95] It is likely that antimicrobial surfaces with biocidal activity could also be used to reduce or eliminate surface contamination in laboratories as well; however, there is a need for data regarding their efficacy against a variety of microorganisms to inform their use in these settings. Experiments should be carried out with different types of antimicrobial surfaces and various pathogen types (e.g., bacteria, viruses, fungi, etc.) in a variety of

presentations (e.g., wet, dry, in culture medium, etc.). Once a given antimicrobial surface has been found effective against a specific biological agent, several laboratories should repeat the efficacy testing to validate efficacy of the surface.

Table 50. Notional Research Design for Efficacy and Validation of Antimicrobial Surfaces

Research Goal	To generate data on the efficacy of antimicrobial surfaces for decontamination of various pathogens
Key Variables	• Antimicrobial surface type (e.g., impregnated or coated with metallic nanoparticles, patterned, functionalized, etc.) • Biological agent type, presentation, and concentration • Efficacy of surface after cleaning • Sampling method (e.g., swabs, RODAC plates, etc.) and scheme (e.g., testing schedule, sampling location, etc.)
Example Protocol	1. Inoculate surface with a known concentration of the chosen pathogen in the selected presentation. 2. Use the sampling method and scheme to determine the efficacy of agent inactivation over time. 3. If a given antimicrobial surface is found to be effective against a specific biological agent, validate its efficacy by repeating a sufficient number of times.
Experimental Outputs	Validated use of antimicrobial surfaces for inactivation of various pathogens
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Aranega-Bou P et al. (2023) Laboratory evaluation of a quaternary ammonium compound-based antimicrobial coating used in public transport during the COVID-19 pandemic. *Appl Environ Microbiol.* 89 (3)**:** e0174422. • Campos MD et al. (2016) The activity of antimicrobial surfaces varies by testing protocol utilized. *PLoS ONE.* 11 (8)**:** e0160728. • Cunliffe AJ et al. (2021) How do we determine the efficacy of an antibacterial surface? A review of standardised antibacterial material testing methods. *Antibiotics (Basel).* 10 (9). • International Organization for Standardization (ISO). (2011) ISO 22196:2011 Measurement of antibacterial activity on plastics and other non-porous surfaces. Switzerland: International Organization for Standardization. • Ojeil M et al. (2013) Evaluation of new in vitro efficacy test for antimicrobial surface activity reflecting UK hospital conditions. *J Hosp Infect.* 85 (4)**:** 274-281. • Sjollema J et al. (2018) In vitro methods for the evaluation of antimicrobial surface designs. *Acta Biomater.* 70**:** 12-24.

5.4. Data Needs for Sustainable Decontamination Methods

5.4.1. Decreasing the toxic by-products produced by incineration of biomedical wastes

A variety of methods (e.g., autoclaving, incineration, microwave treatment, chemical treatment, etc.) exist for decontamination of biomedical wastes; however, incineration remains a popular choice, particularly in resource constrained settings, due to its ease of use and affordability in comparison to other methods.[96,97] Unfortunately, incineration of biomedical wastes can lead to environmental pollution and may have negative impacts on human health.[98] For example, incineration of plastics contained in biomedical wastes often results in emission of air pollutants and the ash that remains

after burning is a major source of dioxin and mercury pollution.[61,99-101] Resource limitations in countries where incineration of biomedical waste is popular may not allow for the purchase of newer alternative treatment methods, such as autoclaves, or the installation of pollution control systems specifically designed for incinerators. Thus, there is a need for development of low-cost strategies that effectively reduce the toxic by-products produced by the biowaste incineration process. Such strategies may include improvement of the incineration process (e.g., increasing burn temperature, alternative fuel source, etc.) to reduce the production of hazardous substances, development of filters to decrease the emission of air pollutants, and containment or remediation of incinerator ash to remove toxins prior to disposal.

Table 51. Notional Research Design for Decreasing the Toxic By-products Produced by Incineration of Biomedical Wastes

Research Goal	To generate data on strategies to reduce the toxic by-products produced by incineration of biomedical wastes
Key Variables	• Wastes being incinerated (e.g., plastics, glass, metal, paper, etc.) • Incinerator type and treatment parameters (e.g., temperature, time, fuel source, etc.) • Pollution reduction strategy (e.g., filtration of exhaust, installation of scrubbers, containment of ash, ash remediation, etc.) and use parameters • Sampling method and scheme
Example Protocol	1. Incinerate waste under typical conditions. 2. Use sampling method and scheme to quantify target pollutant in exhaust or ash. 3. Implement pollution reduction strategy and incinerate waste. 4. Determine ability of strategy to reduce pollution by quantifying target pollutant in incinerated waste. 4. If pollution production is reduced, perform large scale studies to refine process parameters and validate use of the strategy.
Experimental Outputs	Low-cost strategies to reduce the toxic by-products produced by incineration of biomedical wastes
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Kaur H, Siddique R, Rajor A. (2022) Removal of alkalinity and metal toxicity from incinerated biomedical waste ash by using Bacillus halodurans. *Bioremed J.* 26 (1)**:** 1-19. • Suresh Kumar A et al. (2021) Reduction of hazardous incinerated bio-medical waste ash and its environmental strain by utilizing in green concrete. *Water Sci Technol.* 84 (10-11)**:** 2780-2792. • Traina G, Morselli L, Adorno GP. (2007) Electrokinetic remediation of bottom ash from municipal solid waste incinerator. *Electrochimica Acta.* 52 (10)**:** 3380-3385. • Zhang Y et al. (2020) Review of harmless treatment of municipal solid waste incineration fly ash. *Waste Dispos Sustain Energy.* 2 (1)**:** 1-25.

5.5. Data Needs for Combination Methods for Decontamination

5.5.1. Efficacy and validation of combination treatments for decontamination

Current editions of the *BMBL* and the *LBM* recommend that biological wastes be treated by a validated means of decontamination prior to disposal; however, no specific method is prescribed.[11,12] For this reason, most laboratories have developed lab-specific decontamination protocols that employ chemical decontamination methods, non-chemical decontamination methods, or a combination of the two. For example, many labs use chemical treatment and autoclaving while

others may utilize chemical treatment, autoclaving, and incineration depending on the materials to be treated.[12] Single treatment decontamination protocols are often tested and validated; however, there is a lack of data regarding the additive effects of combination protocols. For instance, pre-treatment of a material with a chemical disinfectant may reduce the time needed to fully decontaminate the material via autoclaving. As such, these studies could reduce the time and resources required for decontamination using mixed methods. Experiments should be carried out with a variety of pathogen types (e.g., bacteria, virus, fungus, etc.) in different matrices (e.g., dry vs. liquid waste, carcasses, etc.) and with a variety of treatment combinations (e.g., chemical disinfection & autoclaving, UV irradiation & chemical disinfection, copper nanoparticles & autoclaving, etc.).

Table 52. Notional Research Design for Efficacy and Validation of Combination Treatments for Decontamination

Research Goal	To generate data on the efficacy of combination methods for decontamination of microbes
Key Variables	• Biological agent type, presentation, and concentration • Waste or contaminated material/matrix type • Treatment methods in combination • Treatment parameters for each decontamination method (e.g., chemical concentration, UV wavelength, exposure time, etc.) • Sampling method and scheme
Example Protocol	1. Inoculate waste/material with a known concentration of the target biological agent. 2. Expose to the first treatment method using the chosen parameters. 3. Use sampling method and scheme to determine the concentration of surviving agent. 4. Expose to the second treatment using the chosen parameters. 5. Use sampling method and scheme to recover surviving agent. If survivors are found, adjust treatment parameters until no surviving organisms are present. 6. Validate the decontamination protocol by repeating a sufficient number of times.
Experimental Outputs	Validated combination decontamination method for a given biological agent
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Mourya DT et al. (2016) Use of hydrogen peroxide vapour & plasma irradiation in combination for quick decontamination of closed chambers. *Indian J Med Res*. 144 (2): 245-249.

5.6. Data Needs for Reuse after Decontamination

5.6.1. Contamination of PPE during common laboratory procedures

As a first step toward determining the applicability of PPE decontamination and reuse in research labs, there is a need for real-world data regarding the type, location, and amount of contamination found on the PPE worn by personnel during laboratory procedures. These studies should assess contamination of different PPE types (e.g., body coverings, surgical masks, respirators, PAPR hoods, gloves, shoe covers, rubber boots, etc.) used during a variety of common (e.g., pipetting, culture inoculation, waste processing, etc.) and specialized (e.g., animal handling and infection, cage changes, etc.) laboratory procedures.

Table 53. Notional Research Design to Characterize Contamination of PPE During Laboratory Procedures

Research Goal	To generate data on the rates, types, and locations of contamination of PPE worn during laboratory procedures

Table 53. Notional Research Design to Characterize Contamination of PPE During Laboratory Procedures	
Key Variables	• Biological agent or surrogate organism type and concentration • PPE type and construction material (e.g., nitrile vs. latex gloves, fabric vs. Tyvek lab coat, etc.) • Specific laboratory procedure assessed • Human factors related to performance of laboratory procedure (e.g., pressure or force used, correct use of equipment, etc.) • Sampling method and scheme
Example Protocol	1. Don selected PPE and perform laboratory procedure with selected biological agent/surrogate or fluorescent dye. 2. Use sampling method and scheme to test for presence of contamination on PPE. 3. Repeat a sufficient number of times to calculate the rates of PPE contamination during laboratory procedures.
Experimental Outputs	Rates, types, and location of contamination of PPE during laboratory procedures to inform development of effective decontamination and reuse procedures
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Yarbrough Melanie L et al. (2018) Frequency of Instrument, Environment, and Laboratory Technologist Contamination during Routine Diagnostic Testing of Infectious Specimens. *J Clin Microbiol.* 56 (6)**:** 10.1128/jcm.00225-00218. • Wyneken H et al. (2023) Frequency of Leaks from Conical Centrifuge Tubes. *Appl Biosaf.* 29(1): 1-9. • Wyneken HL et al. (2023) Rate of Splashes When Opening Microfuge Tubes with Various Methods. *Appl Biosaf.* 28 (2)**:** 123-129.

5.6.2. Decontamination of PPE and impacts on performance

In response to the PPE shortages that occurred during the COVID-19 pandemic, many researchers tested methods for decontamination of various disposable PPE items and the impacts that these decontamination procedures had on the efficacy of the PPE for repeated use.[102-106] The vast majority of these studies were conducted to determine the applicability of PPE decontamination and reuse in healthcare settings; as such, there is a need for similar studies to test the decontamination and reuse of PPE worn in laboratory settings where different hazards (e.g., higher concentrations of biological agents, different PPE wear times, chemical exposure, etc.) may be present. Experiments should be conducted with variety of biological agents (or combinations of agents) and various decontamination methods (e.g., exposure to vaporized hydrogen peroxide or other chemical disinfectants, heat/steam treatment, UV irradiation, etc.) to identify an effective method for decontamination of a specific PPE item. Additionally, studies should assess the impact of the decontamination method on the performance of the PPE item and determine the number of decontamination and reuse cycles that a PPE item can undergo before performance is lost.

Table 54. Notional Research Design for Decontamination of PPE for Reuse	
Research Goal	To generate data on the decontamination of PPE items and impacts of decontamination procedures on performance of PPE during reuse
Key Variables	• Biological agent or surrogate organism type and concentration • PPE item (e.g., gloves, respirators, PAPR hoods, body coverings, boots, etc.) and performance metrics (e.g., physical & mechanical properties of medical gloves, filtration efficiency & fit of fitted facepiece respirators, etc.)

Table 54. Notional Research Design for Decontamination of PPE for Reuse	
	• Decontamination method and parameters (e.g., chemical concentration, temperature, exposure time, etc.) • Number of decontamination and reuse cycles • Sampling method and scheme
Example Protocol	1. Contaminate PPE item with a known concentration of the target biological agent or surrogate. 2. Expose the contaminated PPE to the selected decontamination methods using various parameters. 3. Attempt to recover the target organism or surrogate to determine protocol parameters that effectively kill the target organism. 4. Once an effective decontamination protocol is developed, repeat the decontamination procedure on the PPE item, assessing performance of the PPE item after each decontamination cycle, until performance of the PPE items falls below the acceptable threshold. 5. Validate the decontamination protocol efficacy and appropriate reuse conditions by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for decontamination and reuse of a specific PPE item contaminated with a specific biological agent
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Esmizadeh E et al. (2021) Can medical-grade gloves provide protection after repeated disinfection? *ACS Appl Polm Mater.* 3 (1)**:** 445-454. • Esmizadeh E et al. (2021) Stability of nitrile and vinyl latex gloves under repeated disinfection cycles. *Mater Today Sustain.* 11-12**:** 100067. • Grillet AM et al. (2020) COVID-19 global pandemic planning: performance and electret charge of N95 respirators after recommended decontamination methods. *Exp Biol Med.* 246 (6)**:** 740-748. • Grinshpun SA, Yermakov M, Khodoun M. (2020) Autoclave sterilization and ethanol treatment of re-used surgical masks and N95 respirators during COVID-19: impact on their performance and integrity. *J Hosp Infect.* 105 (4)**:** 608-614. • Jung J et al. (2021) Fit-failure rate associated with simulated reuse and extended use of N95 respirators assessed by a quantitative fit test. *Infect Control Hosp Epidemiol.* 42 (11)**:** 1313-1317. • Ontiveros et al. (2021) Assessing the impact of multiple ultraviolet disinfection cycles on N95 filtering facepiece respiratory integrity. *Sci Rep*. 11(1): 12279. • Viscusi DJ et al. (2009) Evaluation of five decontamination methods for filtering facepiece respirators. *Ann Occup Hyg.* 53 (8)**:** 815-827.

5.6.3. Decontamination of laboratory consumables and impacts on performance

Prior to the advent of disposable plastic laboratory consumables, labs regularly decontaminated and reused consumables made of glass or metal. Utilization of these single-use items is advantageous for well-resourced labs because it eliminates the need for time and personnel to process (i.e., decontaminate, wash, and sterilize) reusable items; however, this may not be the case in resource-limited settings where funds are not available for purchase of sustainable glass and/or metal consumables or one-time use of disposable items.[107] Researchers have already demonstrated that reuse of single-use plastic consumables can reduce both the costs of lab operations and the environmental impacts associated with their use; however, there is a need for development of effective decontamination protocols for these items and real-world data regarding the impacts of these decontamination procedures on their repeated use.[107,108] Experiments should be conducted with variety of biological agents (or combinations of agents) and various decontamination methods

(e.g., exposure to vaporized hydrogen peroxide or other chemical disinfectants, heat/steam treatment, UV irradiation, etc.) to identify an effective method for decontamination of a specific consumable (e.g., plastic inoculating loops & spreaders, conical tubes, microcentrifuge tubes, pipette tips, petri dishes, etc.). Additionally, studies should assess the impact of the decontamination method on the performance of the consumable item and determine the number of decontamination and reuse cycles that the item can undergo before performance is lost.

Table 55. Notional Research Design for Decontamination of Laboratory Consumables for Reuse

Research Goal	To generate data on the decontamination of disposable laboratory consumables and impacts of decontamination procedures on their performance during reuse
Key Variables	• Biological agent or surrogate organism type and concentration • Consumable item and performance metrics (e.g., no collapse of plastic tubes, ability to maintain seal, etc.) • Decontamination method and parameters (e.g., chemical concentration, temperature, exposure time, etc.) • Number of decontamination and reuse cycles • Sampling method and scheme
Example Protocol	1. Contaminate consumable item with a known concentration of the target biological agent or surrogate. 2. Expose the contaminated item to the selected decontamination methods using various parameters. 3. Attempt to recover the target organism or surrogate to determine protocol parameters that effectively kill the target organism. 4. Once an effective decontamination protocol is developed, repeat the decontamination procedure on the consumable item, assessing performance of the item after each decontamination cycle, until performance of the item falls below the acceptable threshold. 5. Validate the decontamination protocol efficacy and appropriate reuse conditions by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for decontamination and reuse of a specific laboratory consumable contaminated with a specific biological agent
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Alves J et al. (2021) A case report: insights into reducing plastic waste in a microbiology laboratory. *Access Microbiol.* 3 (3)**:** 000173.

5.6.4. Techno-economic analysis of reuse of PPE and laboratory consumables

Implementation of a sustainability program in which PPE and/or laboratory consumables are decontaminated and reused may result in reduced running costs for the laboratory. As such, there is a need for performance of techno-economic analyses to ensure that these programs produce the desired cost savings. These analyses should consider all factors related to the costs of the items themselves as well as the costs associated with the decontamination and reuse of the items. These decontamination and reuse factors include, but are not limited to, the number of decontamination and reuse cycles for each item, decontamination costs, costs of utilities (e.g., water, electricity, etc.) needed for processing, and personnel hours for washing, treatment, and repackaging of items.

Table 56. Notional Research Design for Cost Savings Associated with Decontamination and Reuse of PPE and Laboratory Consumables	
Research Goal	To generate data on the cost savings associated with implementation of a sustainability program involving decontamination and reuse of PPE and other laboratory consumables
Key Variables	• PPE/Consumable item cost • Item usage rate (e.g., number of items used per month or year) • Number of decontamination and reuse cycles for each item • Decontamination costs (e.g., chemical disinfectants, decontamination equipment, chemical waste disposal, etc.) • Utility costs • Personnel costs
Example Protocol	1. For costs associated with conventional use, use item purchase price and usage rate to determine cost for one time use of items over a specified time period. 2. For sustainability program costs, use initial item purchase price, usage rate, number of decontamination and reuse cycles before disposal, and costs associated with decontamination and preparation for reuse (e.g., decontamination costs, utility costs, & personnel costs) to determine the costs for reuse of items over a specified time period. 3. Implement proposed sustainability program if costs of decontamination and reuse is less than those associated with conventional use of the target PPE and/or consumable items.
Experimental Outputs	Laboratory-specific cost analysis for implementation of a sustainability program involving decontamination and reuse of PPE and other laboratory consumables
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Chu J et al. (2021) Thinking green: modelling respirator reuse strategies to reduce cost and waste. *BMJ Open.* 11 (7)**:** e048687. • Farley M, Nicolet BP. (2023) Re-use of laboratory utensils reduces CO2 equivalent footprint and running costs. *PLoS ONE.* 18 (4)**:** e0283697. • Tao Y, You F. (2021) Can decontamination and reuse of N95 respirators during COVID-19 pandemic provide energy, environmental, and economic benefits? *Appl Energy.* 304**:** 117848.

6. Research Opportunities Related to Waste Management

6.1 Data Needs for Waste Disposal Practices

6.1.1. Interventions/Incentives to increase adherence to waste disposal regulations or best practices

The treatment and disposal of biological wastes by laboratories around the world is typically governed by local and/or national regulations or best practices; however, compliance with these regulations or best practices is not always consistent. In these cases, the implementation of incentive-based programs may improve adherence with regulations and/or best practices for the treatment and disposal of biohazardous wastes.[109] As such, there is a need for real-world data regarding blockers that impede compliance with waste disposal practices, interventions (e.g., incentive programs, training, etc.) to increase compliance, and the development of effective incentive programs. Key variables for these studies include information about the biological agents used in laboratories and health facilities, the types of biohazardous wastes generated, the waste treatment and disposal capabilities of each facility, as well as the interventions (e.g., color coding of waste bins, nudges, visual reminders, enforcement activities, etc.) and/or incentives (e.g., monetary payments,

tax credits and other subsidies, etc.) that would encourage adherence to waste disposal practices in that locale.

Table 57. Notional Research Design for Intervention/Incentive Programs to Increase Compliance with Waste Disposal Regulations or Best Practices

Research Goal	To generate data to inform the development of an incentive program to increase compliance with waste disposal best practices
Key Variables	• Biological agents used and types of biohazardous waste generated • Waste treatment and disposal capabilities • Best practices for treatment and disposal of identified wastes (e.g., segregation, packaging, labeling, etc.) • Blockers that impede compliance with regulations or best practices • Level of staff training in biological waste management • Interventions implemented to increase compliance and/or incentives offered
Example Protocol	1. Identify labs that transport biological waste to an offsite waste treatment facility. 2. Measure how often waste is packaged improperly under existing operating conditions for each lab to establish baseline. 3. Determine the types of interventions/incentives to evaluate and divide labs into the respective number of groups needed. 4. Provide labs with notice of the program's implementation, the program timeline, and the intervention/incentive that their group will receive for compliance. 5. Train personnel from all labs in proper procedures for packaging of biological materials for transport. 6. Check materials delivered to treatment site for proper packaging to determine rates of improper packaging and measure rates of compliance per lab. 7. At the end of the program timeline, calculate the rate of improvement in proper packaging over the baseline compliance for each lab. 8. Compare change in compliance across intervention/incentive groups to assess which correlated with improved waste packaging. 9. Repeat program implementation with the top performing interventions/incentives in a new set of labs to determine effect on compliance in a new locale.
Experimental Outputs	Location-specific intervention/incentive program to increase adherence to treatment and disposal of biohazardous wastes practices
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Alrabiah H, Ahmed V, Bahroun Z. (2025) A systematic review of waste management practices in the healthcare sector. *Clean Waste Syst* 12 (1). • Osei-Tutu B et al. (2025) Adherence to healthcare waste management protocols in selected health facilities, greater Accra and eastern regions, Ghana, 2021. *Discov Environ* 3 (26). • Ozer I. (2013) Tangible incentive programs improve safety results. *Occup Health Saf.* 82 (6): 40, 42, 44.

6.2 Data Needs for Carcass Management

6.2.1. Parameters for above-ground burial of carcasses containing biological agents

Above-ground burial (AGB) is a carcass management technique that has been developed to overcome the negative environmental impacts associated with traditional burial and burning of carcasses. Additionally, this method may be useful in resource-limited settings because it does not require

expensive specialized equipment.[110] AGB has been field tested under certain conditions, such as for the disposal of sheep carcasses in Tunisia as well as cattle and swine carcasses in the United States; however, additional experiments are needed to identify and validate appropriate AGB parameters for use in different environments and to ensure pathogen inactivation.[110-112] Experiments should be carried out with carcasses from a variety of animal species and different pathogen types (e.g., bacteria, viruses, fungi, etc.) using various treatments for each AGB parameter (e.g., trench depth, carbon source, plant species used for vegetative cap, etc.). These data will inform the suitability of AGB for disposal of carcasses harboring biological agents in various environments.

Table 58. Notional Research Design for Parameters for Above-Ground Burial of Carcasses Containing Biological Agents

Research Goal	To generate data on the suitability of above ground burial for disposal of carcasses containing biological agents in various environments
Key Variables	• Animal species and carcass size • Biological agent used • Above ground burial parameters (e.g., trench depth, carbon source, vegetative cap, etc.) • Environmental conditions (e.g., soil temperature, relative humidity, local weather conditions, etc.) • Sampling scheme
Example Protocol	1. Bury infected carcass using chosen parameters. 2. Sample various animal tissues initially and on a justifiable schedule to determine the concentration of surviving agent until no viable agent remains. 3. Use data to develop a protocol for AGB disposal of a specific carcass type carrying a specific biological agent in a given environment and validate by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for disposal of carcasses containing a specific biological agent by above-ground burial in a specific environment
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Ebling R et al. (2022) Virus viability in spiked swine bone marrow tissue during above-ground burial method and under in vitro conditions. *Transbound Emerg Dis.* 69 (5)**:** 2987-2995. • Flory GA et al. (2017) Aboveground burial for managing catastrophic losses of livestock. *Int J One Health.* 3**:** 50-56.

6.2.2. Parameters for composting of carcasses containing biological agents

Composting is a controlled process that decomposes organic materials into a soil-like substance without the negative environmental impacts associated with traditional burial and burning of carcasses. The process can completely break down animal carcasses and is an effective means of pathogen inactivation.[113,114] Composting may be especially useful in resource-limited settings because it does not require expensive specialized equipment.[113] Composting is a well-established carcass disposal method; however, there is a need for validated composting procedures that reliably inactivate a given pathogen in a specific carcass type and ambient environment.[113,115] Experiments should be carried out with carcasses from a variety of animal species and different pathogen types (e.g., bacteria, viruses, fungi, etc.) using various treatments for each composting parameter (e.g., carbon source selection, water use, compost pile mixing and aeration times, etc.). These data will inform the suitability of composting for disposal of carcasses harboring biological agents in various environments.

Table 59. Notional Research Design for Parameters for Composting Carcasses Containing Biological Agents	
Research Goal	To generate data on the suitability of composting for disposal of carcasses containing biological agents in various environments
Key Variables	• Animal species and carcass size • Biological agent used • Composting parameters (e.g., carbon source selection, water use, pile mixing and aeration times, etc.) • Environmental conditions (e.g., soil temperature, relative humidity, local weather conditions, etc.) • Sampling scheme
Example Protocol	1. Compost infected carcass using chosen parameters. 2. Sample various tissues initially and on a justifiable schedule to determine the concentration of surviving agent until no viable agent remains. 3. Use data to develop a protocol for disposal of a specific carcass type carrying a specific biological agent in a given environment by composting and validate by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for composting of carcasses containing a specific biological by above-ground burial in a specific environment
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Kalbasi A et al. (2005) Carcass composting for management of farm mortalities: A Review. *Compost Sci Util.* 13 (3)**:** 180-193. • Payne J, Pugh B. (2017) ANSI-8220: On-Farm Mortality Composing of Livestock Carcasses. Prepared for Oklahoma Cooperative Extension Service. https://pods.okstate.edu/fact-sheets/ANSI-8220pod.pdf. • Wilkinson KG. (2007) The biosecurity of on-farm mortality composting. *J Appl Microbiol.* 102 (3)**:** 609-618.

6.2.3. Addition of decomposers to increase the efficiency of composting carcasses containing biological agents

Composting is a controlled process that decomposes organic materials into a soil-like substance without the negative environmental impacts associated with traditional burial and burning of carcasses. The process can completely break down animal carcasses and is an effective means of pathogen inactivation.[113,114] Composting is often used in resource-limited settings because it does not require expensive specialized equipment. However, the process can take over 12 months to fully decompose carcasses from large animals, and labor is required to manage the composting pile throughout that time.[113,115] As such, identifying methods or additives that can speed up the composting process would result in efficiency and cost savings. One method that may hasten the time required for decomposition is the purposeful addition of decomposing organisms in the early stages of the carcass composting process. Experiments should be carried out with carcasses from a variety of animal species and different pathogen types (e.g., bacteria, viruses, fungi, etc.) using various decomposers (e.g., bacteria, fungi, insects, worms, etc.).

Table 60. Notional Research Design for Addition of Decomposers to Increase the Efficacy of Carcass Composting	
Research Goal	To generate data on the ability of decomposing organisms to increase the efficiency of composting for disposal of carcasses containing biological agents

Table 60. Notional Research Design for Addition of Decomposers to Increase the Efficacy of Carcass Composting	
Key Variables	• Animal species and carcass size • Biological agent used • Decomposer type and concentration • Composting parameters (e.g., carbon source selection, water use, pile mixing and aeration times, etc.) • Location parameters (e.g., soil type, moisture level, etc.) • Environmental conditions (e.g., soil temperature, relative humidity, local weather conditions, etc.) • Sampling method and scheme
Example Protocol	1. Compost two infected carcasses using the chosen parameters with the selected decomposer added to one carcass. 2. For each carcass, sample various tissues initially and on a justifiable schedule to determine the concentration of surviving agent until no viable agent remains. 3. Continue to check carcasses on a set schedule to determine length of time required to reach full decomposition. 4. If addition of decomposers speeds up the decomposition process, use data to develop a protocol for disposal of a specific carcass type carrying a specific biological agent in a given environment by composting with the addition of decomposers and validate by repeating a sufficient number of times.
Experimental Outputs	Validated protocol for decomposer-assisted composting of carcasses containing a specific biological agent in a specific environment
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Kalbasi A et al. (2005) Carcass composting for management of farm mortalities: a review. *Compost Sci Util.* 13 (3)**:** 180-193. • Payne J, Pugh B. (2017) ANSI-8220: On-Farm Mortality Composing of Livestock Carcasses. Prepared for Oklahoma Cooperative Extension Service. https://pods.okstate.edu/fact-sheets/ANSI-8220pod.pdf. • Wilkinson KG. (2007) The biosecurity of on-farm mortality composting. *J Appl Microbiol.* 102 (3)**:** 609-618.

Data Needs and Notional Study Designs for Containment Infrastructure

7. Research Opportunities Related to Laboratory Design and Operations

7.1 Data Needs for Laboratory Design

7.1.1 Upfront life cycle cost analysis for containment laboratories

There are many resources that provide detailed information regarding the costs associated with design and construction of laboratories; however, information regarding the total costs associated with upkeep and operation of laboratories over their lifespans is lacking.[116,117] As such, there is a need for life cycle cost estimates for laboratories of different levels to provide a realistic picture of the budget required to keep these laboratories operational after they are built. Additionally, there is a need for cost estimates that compare the long-term costs associated with initial installation and/or use of low budget construction materials, paints or coatings, and equipment to the lifespan costs associated with their mid-quality and top-of-the-line counterparts. These cost estimates should include the costs associated with the initial purchase of the material/equipment and its installation as well as those related to maintenance, certification, and eventual replacement. Depending on the specific study conducted, lifecycle costs may be reported on a per item or per square foot basis.

Table 61. Notional Research Design for Life Cycle Cost Analysis for Containment Laboratories

Research Goal	To generate data on the life cycle costs for construction materials and equipment used in containment laboratories of different containment and resource levels
Key Variables	• Laboratory containment level (e.g., CL1-4, PC1-4, BSL1-4, ABSL1-4, BSL1-4P, ABSL2-4Ag, ACL1-4, etc.) and associated requirements • Quality of installed construction materials (e.g., flooring, wall coverings, etc.) and equipment (e.g., HVAC system, BSCs, autoclaves, etc.) • Quality of installation and adherence to manufacturer recommendations (e.g., use of recommended cleaners and/or primers to installation, installation in correct conditions [e.g., temperature and relative humidity requirements], appropriate drying and/or curing times, etc.) • Material/equipment-specific maintenance and certification costs (e.g., annual decontamination and certification of BSCs, annual HVAC testing in high-containment labs, etc.) • Utility (e.g., water, gas, electricity, etc.) costs • Costs of annual planned preventative maintenance, including spare parts and consumables • Costs of annual unplanned maintenance • Costs for maintenance and/or replacement of building operation and security equipment and associated software (e.g., building automation system [BAS], card readers, mag locks, etc.) • Estimated lifespan of installed materials/equipment
Example Protocol	1. For a given material or piece of equipment, perform a life cycle cost estimate by determining costs associated with the following: a) Purchase, acquisition, and installation of the item; b) Operation (e.g., required utilities, consumables, etc.); c) Preventative maintenance and certification (e.g., direct costs, materials, and required labor); and d) Disposal costs. 2. Aggregate life cycle costs determined in step one to identify a total lifecycle cost for the specific laboratory-level in question in the given location.

Table 61. Notional Research Design for Life Cycle Cost Analysis for Containment Laboratories	
	3. Use individual item and/or total life cycle costs to compare the costs and benefits of construction materials and equipment of different types and qualities.
Experimental Outputs	Evidence-based life cycle cost estimates for containment laboratories, construction materials, and equipment in a given location
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Fuller S. (2016) Life-Cycle Cost Analysis (LCCA). https://wbdg.org/resources/life-cycle-cost-analysis-lcca. Archived: https://web.archive.org/web/20240701154310/https://wbdg.org/resources/life-cycle-cost-analysis-lcca. Accessed July 1, 2024. • Khare A et al. (2023) Impact of life cycle costing in procurement of robotic track-based central laboratory at Apex Medical Institute in India. *J Lab Physicians.* 15 (4)**:** 539-544. • Martinko K. (2010) Application Note: 01003 - How Understanding the Total Cost of Ownership of Your Instrumentation or Equipment Can Reduce Costs, Increase Performance and Improve Workforce Productivity. Prepared for Thermo Fisher Scientific. https://assets.thermofisher.com/TFS-Assets/CMD/Application-Notes/D19487~.pdf. • University of Virginia. (2024) Life Cycle Cost Calculator https://sustainability.virginia.edu/life-cycle-cost-calculator. Accessed July 1, 2024.

7.1.2. Improved sizing and layout of laboratory anterooms

An anteroom is a small room installed between a clean corridor and a high- or maximum-containment (i.e., [A]BSL3 or [A]BSL4) laboratory to provide a double-door entry into these spaces.[11,12] Furthermore, anterooms provide a barrier between the control measures (e.g., access controls, PPE use, negative airflow and pressure cascade, etc.) implemented in the containment laboratory and the surrounding building and are often used for storage of clean supplies and rarely used items that must be stored near the laboratory, clothing changes, PPE donning and doffing, and shower-out procedures.[11,12,118] Despite the important and variable uses of anterooms, there are no specific guidelines or recommendations for anteroom sizing, and they often end up being too small for their intended uses. Thus, studies are needed to determine the optimal size of an anteroom based on its intended use. When determining optimal sizing, long-term maintenance needs and operations of the entire space/facility should also be considered. These studies should account for different anteroom usage profiles; for example, an anteroom that is used for donning and/doffing of PPE by up to two laboratorians at one time versus an anteroom that is used for donning/doffing of PPE by up to two laboratorians at one time and must store enough PPE for two lab workers for three months as well as house clothing change stalls, a personal shower, and a handwashing sink.

Table 62. Notional Research Design for Improved Sizing and Layout of Laboratory Anterooms	
Research Goal	To generate data on the minimum size and optimal layout of an anteroom based on its intended use

Table 62. Notional Research Design for Improved Sizing and Layout of Laboratory Anterooms	
Key Variables	• Containment level (e.g., CL, PC, BSL, ABSL, etc.) of attached laboratory and types of work conducted in attached laboratory space (e.g., benchwork, use of animals, etc.) • Intended use of anteroom (e.g., change room, pass through vestibule for large equipment, personal shower location, PPE donning/doffing location, PPE storage location, etc.) • Parameters for each use (e.g., number of people changing or donning/doffing PPE at the same time, amount, and types of PPE to be stored, PPE storage method) • Items/Equipment required in anteroom (e.g., hand washing sink, autoclave, eye wash, chemical shower, number and type of electrical outlets, mirror for donning PPE, etc.) • Types and location of storage (e.g., cabinets, adjustable shelving, etc.) • Amount of space required for each material, piece of equipment, or action
Example Protocol	1. To obtain starting guidelines for reasonable sizes, contents, and layouts for anterooms, conduct a survey of the size of existing anterooms in various countries/regions, what they're used for, what they contain, and challenges with the room space and/or layout of each. 2. Determine the various uses that the anteroom will serve and the parameters for each use (e.g., the pieces of equipment that will be in the room, how many people will use the room at once, the actions that will take place in the room, how much PPE will be stored in the space, etc.). 3. Determine the minimum amount of space required for equipment, stored materials, and personnel activities. Aggregate space needs for each item/activity to determine a required square footage for an anteroom with the selected use profile. 4. Using the required square footage, determine possible layouts for the anteroom. In a large area, use painter's tape to map out potential layouts for the anteroom on the floor. Have laboratory personnel walk thru procedures in the taped-out area to determine if the space is adequate. Add additional square footage as needed until the mock room functions as desired. 5. Repeat process to determine appropriate sizing and layouts for anterooms with different use profiles.
Experimental Outputs	Evidence-based layout and sizing of anterooms

7.1.3. Optimization of the laboratory layout to maximize safety

Microbiological laboratories are often laid out in a manner that increases the speed with which personnel can complete their work (i.e., the lab is arranged in a manner that favors efficiency).[119,120] However, should an incident lead to the escape of pathogenic material from primary containment, the layout of a laboratory can have an impact on the safety of the personnel working in the lab. For example, computational fluid dynamics (CFD) based modeling and experimentation has demonstrated that the layout of the laboratory influences the movement of bioaerosols throughout the space, the deposition of aerosols on lab surfaces, and the rate of removal of bioaerosols by the facility HVAC system.[121,122] Despite the influence of laboratory layout on safety, data on how to organize the lab to maximize safety is absent. As such, there is a need for data regarding the ways that the layout of microbiological laboratories affects the safety of their operation. Studies should be carried out with a variety of labs with different sizes, layouts, equipment, and workflows so that factors that impede safety in each space can be identified and ameliorated.

Table 63. Notional Research Design for Optimization of the Layout of Laboratory Equipment to Reduce Deposition of Aerosols on Laboratory Surfaces	
Research Goal	To generate data on the impact of the layout of laboratory equipment to reduce the deposition of infectious aerosols on surfaces

Table 63. Notional Research Design for Optimization of the Layout of Laboratory Equipment to Reduce Deposition of Aerosols on Laboratory Surfaces	
Key Variables	• Physical arrangement of doors/windows, laboratory work areas, and permanent equipment • Setup of work areas and placement of movable equipment • Equipment used concurrently • Ventilation system design, type (e.g., mixing ventilation, displacement ventilation, natural ventilation, etc.), and placement of air terminal devices (ATDs) (e.g., supply and exhaust vents, etc.) • Use of comfort cooling devices (e.g., personal fans, etc.) • Biological agent used in aerosol experiments (e.g., non-pathogenic bacterial model, phage, etc.) • Method for measuring bioaerosols (e.g., microbial plate counts, surface sampling, etc.)
Example Protocol	1. Place open agar plates at various locations throughout the laboratory. 2. Set the laboratory in its typical arrangement with equipment running and organize personnel to move throughout the space in regular patterns. 3. Release a bioaerosol containing a known concentration of non-pathogenic bacteria at a single location (e.g., the benchtop, the centrifuge, etc.). 4. Incubate plates at an appropriate temperature for the microorganism used to quantify the deposition of bioaerosols in each sampling location. 5. Rearrange the laboratory benches and equipment that can be moved and repeat experiment to determine equipment placement that minimizes the deposition of aerosols.
Experimental Outputs	Laboratory layout that reduces the deposition of bioaerosols on surfaces and improves the laboratory layout and ventilation design to maximize safety
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Liu Z et al. (2020) Experimental and numerical study of potential infection risks from exposure to bioaerosols in one BSL-3 laboratory. *Build Environ*. 179: 106991. • Liu Z et al. (2020) Effect of equipment layout on bioaerosol temporal-spatial distribution and deposition in one BSL-3 laboratory. *Build Environ*. 181: 107149.

7.2 Data Needs for Construction Materials

7.2.1 Chemical disinfectant compatibility with materials and hardware used in laboratory construction

High- and maximum-containment laboratories (i.e., BSL3 and BSL4) are often decontaminated by fumigation, fogging, or large-scale spray down with a chemical disinfectant. The interior surfaces in these laboratories generally consist of materials that can withstand chemical decontamination; however, the compatibility of some exposed construction materials (e.g., door handles, hinges, HVAC vents, rubber gaskets, paint, etc.) is not always considered. Some disinfectant manufacturers provide compatibility information for their products, and laboratory studies have assessed the compatibility of disinfectants with different materials, but there is no single resource that individuals can use to determine which metals are compatible with the chemical disinfectants that may be used for space decontamination.[73,74] As such, there is a need for development of a compatibility matrix that delineates the chemical disinfectants that can be used to decontaminate these materials without deleterious effects. This study will involve a comprehensive review of the scientific literature and cataloging of the compatibility information available from disinfectant manufacturers to determine those combinations that have already been tested. For those combinations for which compatibility

information is not already available, large- and small-scale laboratory studies can then be carried out to test the effects that a given disinfectant has on various materials.

Table 64. Notional Research Design for Chemical Disinfectant Compatibility with Construction Materials and Hardware

Research Goal	To assess the compatibility of chemical disinfectants used for space decontamination with various construction materials to inform the development of a chemical disinfectant-metal compatibility matrix
Key Variables	• Construction material (e.g., metal [aluminum, copper, nickel, iron, etc.] or alloy composition [steel, brass, bronze, etc.], rubber, etc.) • Chemical disinfectant and use parameters (e.g., chemical concentration, contact time, environmental conditions [ambient temperature and relative humidity], etc.) • Treatment frequency (e.g., annual, etc.) • Environmental conditions (e.g., temperature, relative humidity, etc.) • Method for characterizing surface degradation or corrosion (e.g., nuclear magnetic resonance, optical microscopy, contact angle, atomic force microscopy, weight, etc.) [75,123]
Example Protocol	1. Expose the test metal to the chemical disinfectant using the selected parameters. 2. After treatment, assess the surface of the metal for degradation/corrosion caused by the disinfectant. 3. Repeat the process regularly over the course of the study to determine what, if any, degradative impacts can be associated with continued use of the disinfectant over time.
Experimental Outputs	Compatibility of chemical disinfectants with various metals used in hardware; chemical disinfectant-metal compatibility matrix resource
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Abban S, Jakobsen M, Jespersen L. (2013) A practical evaluation of detergent and disinfectant solutions on cargo container surfaces for bacteria inactivation efficacy and effect on material corrosion. *Afr J Biotechnol.* 12 (23)**:** 3689-3698. • International Organization for Standardization. (2022) ISO 5156:2022 Corrosion of Metals and Alloys - Corrosion Test Method for Disinfectant - Total Immersion Method. Switzerland: International Organization for Standardization. • LANXESS. (2022) Virkon S - Vehicle Disinfection Materials Compatibility. Prepared for LANXESS Corporation. https://www.qcsupply.com/media/product_attachments/attachment_file/v/i/virkon_s_vehicle_disinfectant_compatibility.pdf. • Teska P et al. Characteristics of an Ideal Surface Damage Testing Protocol. https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Archived: https://web.archive.org/web/20240208164254/https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Accessed February 7, 2024.

7.3 Data Needs for Mobile Laboratories

Mobile laboratories are often utilized for on-site diagnostic testing during infectious disease outbreaks.[124-126] Use of these purpose-built structures is especially advantageous in areas that may lack both diagnostic and medical infrastructure.[127,128] Mobile laboratories have been successfully deployed in response to recent outbreaks of Ebola and COVID-19; however, there is a need for empirical evidence related to the layout of these laboratories, and the practices used within them, to ensure that they are utilized in the safest manner possible.[128,129]

7.3.1 Optimization of the mobile laboratory layout for safety

The layout of work areas and equipment in mobile laboratories is often determined by the need to fit the necessary components into a very small space while still allowing for mobility.[129] Biosafety in mobile laboratories, and other space restricted settings, is often accomplished by optimizing the equipment and laboratory practices used in the mobile laboratory; however, it's possible that the physical arrangement of the laboratory components could also impact the safety of its use.[125,130]. Thus, there is a need for data regarding the ways that the layout of space restricted laboratories affects the safety of their operation. Studies should be carried out with a variety of labs with different layouts, equipment, and workflows so that factors that impede safety in each space can be identified and ameliorated.

Table 65. Notional Research Design for Optimization of the Layout of Space Restricted Laboratories for Safety

Research Goal	To generate data on laboratory layout or other elements that impact the safety of operations in space restricted laboratories
Key Variables	• Physical arrangement of laboratory work areas and permanent equipment • Setup of work areas and placement of movable equipment • Laboratory workflow and assays performed • Number of personnel working in laboratory simultaneously
Example Protocol	1. Use video cameras to observe personnel working in the laboratory to identify layout elements that are impediments to safety. 2. If impediments are identified, develop and implement structural changes, modified practices, and/or workarounds and test for their ability to mitigate safety issues.
Experimental Outputs	Space restricted laboratory layout that has been optimized for safety
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Linster M, Ng B, Vijayan V. (2020) COVID-19 and beyond: safety and design considerations for the development of a mobile biocontainment laboratory. *Appl Biosaf.* 25 (3)**:** 169-173. • Rao V, Bordelon E. (2019) Mobile high-containment biological laboratories deployment: opportunities and challenges in expeditionary deployments to outbreak response. *Appl Biosaf.* 24 (1)**:** 20-29.

7.3.2 Safety of practices in mobile laboratories

It is unclear whether factors specific to mobile laboratories (e.g., space and HVAC constraints, inconsistent power, temperature fluctuations, high sample volumes, etc.) impact the degree of safety of the practices designed for use in conventional laboratories. As such, there is a need for empirical data regarding the production of contamination by common laboratory practices when used in the mobile laboratory setting to inform the development of safe lab practices for use in these areas. Additional studies which assess the application of processes used in traditional laboratories (e.g., annual certification of BSCs, etc.) are also needed to inform the safe use of mobile laboratories.

Table 66. Notional Research Design for Contamination Produced During Common Laboratory Practices in Mobile Laboratories

Research Goal	To generate data on the rates and types of contamination produced during common laboratory procedures in the mobile laboratory setting to inform the implementation of mitigations that reduce or prevent contamination

Table 66. Notional Research Design for Contamination Produced During Common Laboratory Practices in Mobile Laboratories	
Key Variables	• Specific laboratory practice to be assessed and equipment/supplies used during practice • Test sample (e.g., water, fluorescent dye, microbial culture, etc.) • Aerosol/droplet sampling method (e.g., particle counter/sizer, microbial settle plates, cassette filters, etc.) • Human factors related to performance of laboratory practice (e.g., pressure or force used, etc.) • Mitigation strategies (e.g., placement of physical barriers, HVAC adjustments, use of primary containment, practice modifications, local exhaust ventilation, etc.)
Example Protocol	1. In the mobile laboratory, perform the chosen practice while sampling for the creation of contamination. 2. If contamination is produced, implement mitigation strategies and test for reduction in the rate of contamination.
Experimental Outputs	Rates and types of contamination produced during common laboratory practices in the mobile laboratory; development of mitigations that reduce or prevent contamination
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Miller HE et al. (2014) Characterization of respirable aerosols generated during routine laboratory procedures. *Appl Biosaf.* 19 (1)**:** 19-27. • Pottage T et al. (2014) Quantification of microbial aerosol generation during standard laboratory procedures. *Appl Biosaf.* 19 (3)**:** 124-131. • Pottage T et al. (2022) Microbial aerosols generated from standard microbiological laboratory procedures. *Appl Biosaf.* 27 (2)**:** 92-99.

7.4 Data Needs for Laboratory Utilities

7.4.1 Cost impact of transitioning a laboratory to an alternative energy source

Laboratories are known to consume large amounts of energy, with the average laboratory facility using up to five to ten times more energy than an office building of the same size.[131-133] With the exception of data centers, laboratories use the highest amounts of energy per square foot of space compared to any other sector and can account for up to 60% of an institution's electricity use.[134,135] Due to this cost, renewable energy sources (e.g., solar energy, wind energy, hydroelectricity, etc.) may be beneficial for laboratories, especially in remote regions where accessing traditional electricity may be difficult. However, it is unclear whether powering a lab using an alternative energy source would result in significant cost savings. Thus, there is a need for an analysis that determines the amount of energy required to operate a given laboratory and then compares the total cost associated with installation, operation, and maintenance of a system capable of running the laboratory using alternative energy to the costs of using a traditional power source. If a switch to alternative power is found to be cost effective, laboratories that are transitioned should include a monitoring mechanism to ensure there are no interruptions in power supply that could cause safety issues.

Table 67. Notional Research Design for Cost Impact of Transitioning a Laboratory to an Alternative Energy Source	
Research Goal	To compare the costs of operating a laboratory using traditional energy to those associated with transition to an alternative energy source

Table 67. Notional Research Design for Cost Impact of Transitioning a Laboratory to an Alternative Energy Source	
Key Variables	• Laboratory size • Laboratory systems in place (e.g., HVAC, access and security systems, etc.), operating profile (e.g., always-on systems vs. stand-by mode, etc.), and operating parameters (e.g., target air pressure, target temperature, target humidity, etc.) • Laboratory equipment used (e.g., BSCs, autoclaves, ultra-low freezers, centrifuges, thermocyclers, microscopes, etc.) and operating profile (e.g., always-on, standby mode, intermittent use, etc.) • Method for determining energy usage (e.g., average usage from utilities statement, use of wattmeter to measure actual energy usage, etc.) • Alternative energy type (e.g., solar, wind, hydroelectricity, etc.), associated equipment (e.g., solar panels, wind turbine, etc.), and maintenance requirements
Example Protocol	1. Select a model laboratory for the analysis and determine the systems and equipment in use. 2. Use the selected method to determine the average amount of energy used by the model laboratory on an annual basis. 3. Work with a commercial vendor to determine the total cost associated with installation, operation, and maintenance of an alternative energy system with capable of providing the energy required by the laboratory. 4. Verify that the alternative source can provide the power supply required to run the laboratory on a consistent basis. 5. Compare the costs of a transition to an alternative energy source to those associated with use of a traditional power source.
Experimental Outputs	Costs associated with transitioning to operating a laboratory using alternative energy; evidence-based selection of laboratory energy source based on cost
Reference Studies	The following publications and tools may serve as references for planning and conducting studies related to this data need: • Hopkinson L et al. (2011) Energy Consumption of University Laboratories: Detailed Results from S-Lab Audits. Prepared for Safe, Successful and Sustainable Laboratories (S-Lab) Initiative of Higher Education for Environmental Performance Improvement (HEEPI) Available from: https://www.mygreenlab.org/uploads/2/1/9/4/21945752/ie_-_energy_consumption_of_univeristy_laboratories_-_s-labs.pdf. • International Institute for Sustainable Laboratories. (2025) Laboratory Benchmarking Tool. Available from: https://lbt.i2sl.org/. Accessed January 16, 2025. • Mathew P et al. (2004) Rating Energy Efficiency and Sustainability in Laboratories: Results and Lessons from the Labs21 Program. Prepared for Lawrence Berkeley National Laboratory. Available from: https://www.osti.gov/servlets/purl/835809. • Royal Society of Chemistry. (2022) Sustainable Laboratories: A Community-Wide Movement Toward Sustainable Laboratory Practices. Available from: https://www.rsc.org/globalassets/22-new-perspectives/sustainability/sustainable-labs/sustainable-laboratories-report.pdf. • Samson AO, Babatunde OM, Denwigwe IH. (2019) Powering a Space Environment Research Laboratory (SERL): Hybrid Renewable Energy System or Diesel System? *J Energy Eng*. 116 (2): 41-64.

7.4.2 Personnel safety during power outages

In accordance with the current editions of the *BMBL*, the *LBM*, and various country-specific standards, BSCs should be connected to an emergency generator or other backup power source in the event that primary power is lost.[11,12,136,137] However, it is unclear if the user protection provided by the BSC is interrupted during the period of transition from the normal power supply to the backup power supply. Experiments should be carried out with various BSC types and brands and different

backup power sources and connections to determine if a loss of containment occurs during the changeover from standard to backup power. If containment is lost during the transitionary period, procedures should be developed and implemented to limit the potential exposure of personnel using BSCs during power failures.

Table 68. Notional Research Design for Loss of BSC User Protection During Transition to Backup Power

Research Goal	To generate data on the user protection provided by BSCs during the transition from standard to backup power
Key Variables	• BSC class/type • Backup power supply type (e.g., generator, uninterruptable power supply, etc.) • Frequency and causes of power outages (e.g., weather event, power instability, etc.) • Number of BSCs/replicates • Method for measuring operator protection (e.g., *Bacillus subtilis* spore test, potassium iodide methods, etc.) [136,137]
Example Protocol	1. With BSC running on standard power, begin measuring operator protection using the chosen method. 2. Transfer BSC to backup power and allow cabinet function to stabilize while continuing to measure operator protection.
Experimental Outputs	% of BSCs with altered operator protection during transition from standard to backup power
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Held KF, Thibeault R, Boudreau J. (2019) Heat sources in a biosafety cabinet compromise experimental and user protection. *Appl Biosaf.* 24 (2)**:** 90-95. • Parks S et al. (2022) The impact of air inflow and interfering factors on the performance of microbiological safety cabinets. *Appl Biosaf.* 27 (1)**:** 23-32.

8. Research Opportunities Related to Engineering Controls and Facility Equipment

8.1 Data Needs Related to Facility Airflow and Air Filtration

8.1.1 Required pressure for directional airflow

The current edition of the *BMBL* recommends that BSL3-BSL4 and ABSL2-ABSL4 laboratories be fitted with a ventilation system that ensures containment and prevents cross contamination by maintaining the laboratory at negative pressure to create inward directional airflow and differential pressure between adjacent laboratory spaces.[11,138,139] Additionally, the *BMBL* recommends that the inclusion of a ventilation system that creates inward airflow be considered when designing BSL2 laboratories for new construction.[11] Despite widescale acceptance that negative pressure and directional airflow are important for ensuring containment, there are very few sources that provide recommended ventilation and exhaust parameters (e.g., negative pressure value, air changes per hour, etc.), and those that do provide values do not align. For example, air changes per hour (ACH) recommended for laboratories range from 4-15 ACH depending upon source.[118,140,141] Similarly, the NIH recommends a negative pressure differential of 12.5 Pascal (Pa) or 0.05 inches of water gauge (0.05” w.g.) while other sources recommend a negative pressure differential without providing a value for the level of negative airflow needed.[118,142] As such, there is a need for a definitive determination of the airflow

parameters (e.g., air changes per hour and pressure differential) needed to maintain containment in laboratory facilities of different types.

Table 69. Notional Research Design for Required Pressure for Directional Airflow	
Research Goal	To generate data on the pressures and flow rates required for directional airflow to ensure laboratory containment
Key Variables	• Lab size and configuration (e.g., number of doors/entries, layout of supply and exhaust vents, etc.) • Ventilation and exhaust system specifications and capabilities • Method for simulating microbial aerosols (e.g., smoke stick/wand, vapor generator, tracer gas, etc.) • Methodology for testing/measuring directional airflow (e.g., differential pressure monitor, airflow velocity meter, etc.) [142,143] • Reliability of measurement equipment (e.g., gauges, sensors, transducers, etc.) • System controllability (e.g., adjacent pressure steps, potential crossover, etc.) • Room leakage
Example Protocol	1. Assess relevant literature sources (e.g., NIH Design Requirement Manual, etc.) to identify pressure values that can serve as a starting point for determining the pressure required for directional airflow. 2. With the lab in a static state (e.g., no air flowing into or out of the laboratory) release a test aerosol near the main entry to the laboratory. 3. While using a differential pressure monitor to measure air pressure, gradually adjust the ventilation system to a starting pressure indicated by literature review. Visually inspect for the creation of negative pressure (i.e., movement of the test aerosol into the laboratory). 4. Continue releasing test aerosol near the entry door until a level of negative pressure that prevents reflux of the aerosol out of the lab is reached. 5. Create test aerosols near other openings and other parts of the room and continue adjusting ventilation to make lab more negative until aerosols created in the room are exhausted without reflux out of the laboratory. 6. Record the pressure value required to create directional airflow into the laboratory and prevent the reflux of test aerosols out of the laboratory. 7. Test the required pressure in labs of different types and configurations, and with different types of equipment in use, to determine if it is applicable to a wide variety of use cases. Individual laboratories can then use this pressure to calculate the needed airflow rate and ACH for ensuring containment in the laboratory.
Experimental Outputs	Evidence based air pressures for directional airflow to ensure containment in laboratories
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • ANSI, ASSP. (2020) ANSI/ASSP Z9.14 - 2020 Testing and Performance-Verification Methodologies for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Ventilation Systems. Park Ridge, Illinois, USA: ASSP. • Bennett AM, Parks SR, Benbough JE. (2005) Development of particle tracer techniques to measure the effectiveness of high containment laboratories. *Appl Biosaf*. 10 (3): 139-150. • Liang L, Hong, X, Lu B, et al. (2022) Comparative analysis of technical requirements for heating, ventilating, and air conditioning (HVAC) systems in high-biocontainment facility standards. *Biosaf Health.* 5 (1): 1-7. • Kurth A, Weber U, Reichenbacher D. (2022) Maintaining differential pressure gradients does not increase safety inside modern BSL-4 laboratories. *Front Bioeng Biotechnol.* 10**:** 953675.

8.1.2 Determination of optimal laboratory ventilation

As mentioned above, highly regarded biorisk management guidelines often recommend that handling of the most severe pathogens (i.e., those that are infectious via the aerosol route and for which treatment may not be available) be conducted in laboratories fitted with a ventilation system that ensures containment of those agents.[11,12,144] Despite these recommendations, there are very few sources that provide ventilation and exhaust parameters for laboratories and even fewer resources to aid individuals in the design of efficient and effective ventilation systems. Thus, there is a need for fundamental studies into the optimization of laboratory HVAC systems, particularly experiments focused on determining what airflow change rates are required to ensure safe ventilation and what variables in a laboratory may change those air change requirements (e.g., a long rectangular room may need more air changes or more exhaust than a square room, etc.). Ultimately, the information obtained from these studies could be used develop standardized guidance and requirements for laboratory HVAC design. These studies would benefit from being conducted in a standardized space so that repeatable experiments, such as those described above, can be carried out to design an optimal system that can then be adapted to a wide range of laboratory use cases.

Table 70. Notional Research Design for Determination of Optimal Laboratory Ventilation

Research Goal	To generate data that informs the optimization of laboratory ventilation systems
Key Variables	• Lab size and configuration (e.g., number of doors/entries, layout of supply and exhaust vents, etc.) • Ventilation and exhaust system specifications and capabilities • Environmental parameters (e.g., temperature, relative humidity, etc.) • Method for simulating microbial aerosols (e.g., smoke stick/wand, vapor generator, tracer gas, etc.) • Methodology for testing/measuring directional airflow (e.g., differential pressure monitor, airflow velocity meter, etc.) [142,143] • Reliability of measurement equipment (e.g., gauges, sensors, transducers, etc.) • System controllability (e.g., adjacent pressure steps, potential crossover, etc.) • Room leakage
Example Protocol	1. Design and commission a laboratory space to be used for ventilation studies. 2. Using the commissioned laboratory space, conduct repeatable experiments to determine ventilation parameters that maintain containment under a variety of laboratory conditions. 3. Use observations and data to design an optimal laboratory ventilation system.
Experimental Outputs	Evidence-based design of laboratory ventilation systems
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Caskey S et al. (2023) Computational fluid dynamics simulations to assess spatial variability and optimal ventilation scenarios for biological laboratory exposures. *Appl Biosaf*. 28 (4): 156-264.

8.1.3 Release of particles from HEPA filters during change procedures

High efficiency particulate air (HEPA) filters are installed in BSCs and some laboratory HVAC systems to trap and contain airborne particles containing biological agents.[145,146] Some HEPA systems have bag-in-bag-out (BIBO) technology that allows contaminated HEPA filters to be removed within a sealed bag to minimize the risk of infectious particles being released into the laboratory environment.[147] For HEPA systems that do not include BIBO technology, BSC standards and industry

guidelines recommend that BSCs undergo gaseous decontamination before HEPA filters are changed.[148] However, it is unclear whether trapped particles are released from HEPA filters during filter change procedures to necessitate the use of BIBO technology or gaseous decontamination prior to filter changes. Thus, there is a need for experimental data regarding how often potentially infectious particles are released from BSC and/or HVAC HEPA filters during filter change procedures.

Table 71. Notional Research Design for Release of Particles from HEPA Filters During Change Procedures

Research Goal	To generate data on the frequency with which particles are released from HEPA filters during change procedures
Key Variables	• HEPA system type (e.g., BSC, HVAC, etc.) • HEPA filter brand • Filter fill level (operating optimally with normal airflow vs. clogged with reduced airflow) • Laboratory type (e.g., clean room, particulate-heavy environment, animal housing space, etc.) • Environmental conditions (e.g., temperature, relative humidity, etc.) • Filter change procedure • Particle sampling device (e.g., particle counter/sizer, microbial settle plates, cassette filters, etc.) and use procedure (e.g., placement, sampling period length and schedule, etc.) • Mitigations to prevent/decrease the release of particles during filter change procedures (e.g., slow movement, immediate bagging of filter, dousing with disinfectant, applying spray glue to fix particles, etc.)
Example Protocol	1. Identify a cohort of HEPA filters for testing. When selecting filters for testing, take the brand, fill level, laboratory type, and environmental conditions into account. 2. Use sampling method to obtain background particle counts in the general area of the HEPA filter. 3. Don appropriate PPE (if required for agents used in the lab) and perform the selected filter change procedure while sampling for airborne particles continuously or on a set schedule (e.g., every 30 seconds, etc.). 4. Compare particle counts obtained during/after the filter change procedure to the background counts to determine if particles were released during the procedure. 5. If particles are released during the procedure, determine efficacy of mitigations intended to prevent or decrease the release of particles during filter change procedures.
Experimental Outputs	Rate of particle release from HEPA filters during change procedures; evidence-based HEPA filter change procedures

8.1.4 Efficacy of HEPA filter decontamination

HEPA filters are installed in BSCs and some laboratory HVAC systems to trap and contain airborne particles containing biological agents.[145,146] Some HEPA systems have bag-in-bag-out (BIBO) technology that allows contaminated HEPA filters to be removed for decontamination and/or destruction off-site. In this process, the filters are removed within a sealed bag to minimize the risk of infectious particles being released into the laboratory environment.[147] In the absence of this BIBO technology, BSC standards and industry guidelines recommend that BSCs undergo gaseous decontamination using formaldehyde, hydrogen peroxide, or chlorine dioxide before internal portions of the BSC are accessed or HEPA filters removed.[136,137,148,149] However, it is unclear whether there is potential for pathogens to persist in the filter after treatment or if decontamination processes effectively inactivate all pathogens trapped in the filter. For this reason, studies are needed to test the efficacy of gaseous decontamination of HEPA filters to determine if additional mitigations are required even after the filters have been decontaminated. Experiments conducted to generate

this data should include all gaseous agents typically used for HEPA filter decontamination and a variety of pathogen types (e.g., bacteria, viruses, fungi, etc.) used in relevant amounts.

Table 72. Notional Research Design for Efficacy of HEPA Filter Decontamination

Research Goal	To generate data on the efficacy of HEPA filter decontamination to inform the need for bag-in-bag-out technology
Key Variables	• Biological agent/surrogate type and concentration • HEPA system type (e.g., BSC, HVAC, etc.) • HEPA filter brand • Filter fill level • Laboratory type (e.g., clean room, particulate-heavy environment, animal housing space, etc.) • Environmental conditions (e.g., temperature, relative humidity, etc.) • Gaseous decontaminant used (e.g., formaldehyde, chlorine dioxide, or hydrogen peroxide) and treatment parameters
Example Protocol	1. Use a known concentration of the selected biological agent/surrogate to contaminate the selected HEPA filter, allow to dry, and install in the BSC or HVAC system. 2. Use the selected fumigant and recommended parameters to decontaminate the HEPA filter. 3. After treatment, access the HEPA filter and attempt to recover the target organism to determine if the fumigant and associated parameters that completely inactivates the target organism. a) If surviving agent is present, adjust the treatment parameters and re-test until the agent is completely inactivated. b) If no surviving agent remains, validate the decontamination method by repeating the process a sufficient number of times. 4. Test the effectiveness of the decontamination method in different environmental conditions (e.g., high/low temperature or relative humidity, etc.) and against different filter brands and/or presentations (e.g., filter filled with animal hair or dander, etc.) to ensure that the method works under a variety of conditions.
Experimental Outputs	Efficacy of HEPA filter decontamination methods; evidence-based recommendation regarding the need for bag-in-bag-out filter containment technology
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • British Standards Institute. (2000) BS EN 12469:2000 Biotechnology - Performance Criteria for Microbiological Safety Cabinets. London, England: British Standards Institute • Czarneski MA, Lorcheim K. (2011) A discussion of biological safety cabinet decontamination methods: formaldehyde, chlorine dioxide, and vapor phase hydrogen peroxide. *Appl Biosaf*. 16 (1): 26-33. • NSF, ANSI. (2022) NSF/ANSI 49-2022 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification. Ann Arbor, Michigan, USA: NSF International. • Thermo Scientific. (2014) Technical Note: Biological Safety Cabinets - Fumigation Methodologies https://assets.thermofisher.com/TFS-Assets/LED/Warranties/BSC-Fumigation-Technical-Note.pdf. Archived: https://web.archive.org/web/20231226090956/https://assets.thermofisher.com/TFS-Assets/LED/Warranties/BSC-Fumigation-Technical-Note.pdf. Accessed January 13, 2025.

8.2 Data Needs for Safe Use of Facility Equipment

8.2.1 Efficacy of locally manufactured BSCS and BSC filters

BSCs are primarily manufactured in the Unites States, Europe, and Asia, and this geographic concentration of manufacturing in only a few areas has forced users in other parts of the world to transport cabinets over long distances at a significant cost.[150] To alleviate this issue, small firms have begun manufacturing BSCs and/or BSC filters in these underserved areas. However, it is unclear whether these items are as effective as those produced by major manufacturers. Thus, there is a need for data regarding the efficacy of BSCs and/or filters manufactured by small local firms. Testing the efficacy of locally manufactured BSCs and/or filters should include confirmation of performance over time. BSC performance metrics tested may include, but are not limited to, filter and filter housing integrity, inflow and downflow velocities, and internal air patterns in accordance with an applicable standard. Similarly, the performance of high-efficiency particulate air (HEPA) and ultra-low particulate air (ULPA) filters may include integrity and leak testing per the chosen performance standard.[136,137]

Table 73. Notional Research Design for Efficacy of Locally Manufactured BSCs

Research Goal	To generate data on the efficacy of locally manufactured BSCs
Key Variables	• BSC class/type • Number of replicates/number of BSCs • BSC performance metrics and associated test methods • Testing timeline • Certification standard (e.g., NSF 49, EN 12469, etc.)
Example Protocol	1. Install investigational (i.e., locally manufactured) and control (i.e., major manufacturer) BSCs and certify in accordance with applicable standard. 2. Conduct selected performance tests not included in the certification process in accordance with applicable standard. 3. Utilize BSCs in accordance with typical laboratory workflow. 4. Recertify BSCs annually and performance test BSCs on a chosen justifiable schedule (e.g., every three or six months) until the chosen end point is reached. 5. Compare performance of investigational BSC to that of the control BSC at chosen time points.
Experimental Outputs	Performance measures of investigational and control BSCs over time; efficacy of locally manufactured BSCs
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Fontaine CP et al. (2010) Novel testing of a biological safety cabinet using PCR. *Appl Biosaf.* 15 (4)**:** 186-196. • Huang RF, Chou CI. (2009) Flow and performance of an air-curtain biological safety cabinet. *Ann Occup Hyg*. 53 (4): 425-440. • Parks S et al. (2022) The impact of air inflow and interfering factors on the performance of microbiological safety cabinets. *Appl Biosaf.* 27 (1)**:** 23-32.

Table 74. Notional Research Design for Efficacy of Locally Manufactured BSC Filters

Research Goal	To generate data on the efficacy of locally manufactured HEPA/ULPA filters
Key Variables	• BSC class/type • Number of replicates/number of filters • Filter performance metrics and associated test methods • Testing timeline • Certification standard (e.g., ISO 29463)

Table 74. Notional Research Design for Efficacy of Locally Manufactured BSC Filters	
Example Protocol	1. Install investigational (i.e., locally manufactured) and control (i.e., major manufacturer) filters in BSCs of the same model and certify in accordance with applicable standard. 2. Utilize both BSCs in accordance with typical laboratory workflow. 3. Recertify BSCs annually and performance test filters on a chosen justifiable schedule (e.g., every three or six months) until the chosen end point is reached. 4. Compare performance of investigational filter to that of the control filter at chosen time points.
Experimental Outputs	Performance measures of investigational and control BSC filters over time; efficacy of locally manufactured HEPA/ULPA filters
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • U.S. National Institutes of Health. (2022) HEPA Air Filtration in Cleanrooms - Design, Construction and Testing Requirements. Technical News Bulletin. (124).

8.2.2 Impact of supplies and equipment inside BSC on airflow disruption

The current editions of both the *LBM* and *BMBL* recommend that supplies and equipment inside the BSC be minimized as their presence may disrupt airflow within the cabinet leading to cross-contamination and/or loss of containment.[11,12] However, experimental data are needed to determine the number and/or types of supplies or equipment that can be used inside a BSC before its function is impacted. Additionally, real-world data are needed to inform the placement of high-motion equipment (e.g., vortex mixers, rotary mixers, etc.) within the BSC to ensure that airflow is not disturbed. The combinations of supplies and equipment used in this testing should be based on real-life scenarios, such as those needed to change rodent cages, extract nucleic acids from bacterial cultures, etc.

Similarly, there are questions about the impacts that multiple users working the cabinet at the same time may have on the BSC's operation. A previous study, that used mannequins to simulate multiple BSC users, found that the presence of two or three individuals can restrict the inflow of air into the cabinet and impact the level of personnel and product protection it provides.[151] However, additional studies are needed to determine the impacts of humans actually working in the BSC and to identify and test practice modifications that could allow multiple users to work in a BSC simultaneously in cases where this practice is necessary (e.g., cage changes, etc.).

Table 75. Notional Research Design for Determination of the Number and Types of Supplies and Equipment Used in a BSC	
Research Goal	To generate data on the number and types of supplies and equipment that can be used in a BSC before its function is negatively impacted
Key Variables	• BSC class/type • Number, types, and placement of supplies and equipment • Method for observing airflow disturbances (e.g., NSF/ANSI 49 smoke tests, etc.) • Placement of high-motion equipment within BSC
Example Protocol	1. Load various combinations of supplies and equipment into the BSC and perform/mime worker activities while using the chosen method to assess for disturbances in airflow. 2. To determine the effects of high-motion equipment on airflow within the BSC, use chosen method to assess for disturbances in airflow while equipment is running.
Experimental Outputs	Appropriate number and types of supplies and equipment for use in a BSC at a given time; appropriate placement of high-motion equipment within the BSC

Table 75. Notional Research Design for Determination of the Number and Types of Supplies and Equipment Used in a BSC	
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Held K, Boudreau J. BSC Myth Busters: Can Overcrowding a BSC Work Area Lead to a Loss of Containment. https://bakerco.com/images/uploads/assets/Overloaded_BSC.pdf.

8.2.3 Determination of minimum required open space in front of BSC to prevent airflow disruptions from personnel traffic in the laboratory

Studies have demonstrated that the airflow within a BSC can be disturbed when an individual walks too closely to the cabinet during use.[152,153] Current editions of the NSF/ANSI 49 standard and the NIH's Design Requirements Manual recommend at least 40 inches of open space in front of the BSC; however, it is unknown whether this recommended distance is sufficient to prevent the generation of airflow disturbances in the cabinet when an individual walks by the BSC while it is in use.[118,137] Researchers have performed experiments to determine that 40 inches of open space in front of a single model of Type II, Class A2 BSC is sufficient to prevent airflow disturbances[154]. However, there is a need for additional reps of these experiments with Type II, Class A2 BSCs from other manufacturers, as well as similar experiments for other types/classes of BSCs to determine an evidence-based recommendation for the minimum required space needed in front of a BSC to ensure that laboratory traffic does not impact cabinet airflow and function. Experiments conducted to provide this data should be conducted with different classes, types, sizes (e.g., four-foot length, six-foot length, etc.) and brands of BSCs, and with individuals walking past the cabinet as varying distances and speeds.

Table 76. Notional Research Design for Minimum Required Open Space in Front of BSC	
Research Goal	To generate data on the minimum required open space in front of a BSC to prevent airflow disruptions from movement of laboratory personnel
Key Variables	• BSC type/class and brand • Amount of open space in front of BSC • Speed and distance of individual walking past cabinet • Method for observing airflow disturbances and/or measuring loss of protection in the BSC (e.g., smoke pattern testing, particle counting inside the BSC, NSF/ANSI 49 personnel protection test, BS EN 12469 operator protection test, etc.) • Traffic parameters (e.g., distance from BSC, speed, arm swinging, etc.)
Example Protocol	1. Set up smoke machine in a position which allows visualization of airflow for chosen BSC. 2. Have participant walk past running BSC at selected distance, speed, etc. while monitoring for airflow disturbances. 3. If airflow is disturbed, increase open space between BSC and traffic until airflow is no longer impacted.
Experimental Outputs	Evidence-based recommendation for minimum open space in front of BSC to prevent airflow disruptions from personnel traffic
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • BSI. (2000) BS EN 12469: Biotechnology - Performance Criteria for Microbiological Safety Cabinets. London, England: British Standards Institute • NSF, ANSI. (2022) NSF/ANSI 49-2022 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification. Ann Arbor, Michigan, USA: NSF International.

Table 76. Notional Research Design for Minimum Required Open Space in Front of BSC	
	• The Baker Company. (2023) BSC Mythbusters - How Much Space is Required Around a Biosafety Cabinet to Maintain Proper Protection [Video]. YouTube. https://www.youtube.com/watch?v=DeWmavEp3wc.

8.2.4 Parameters for UV decontamination of BSCs and efficacy of UV decontamination over time

NSF/ANSI 49 and current editions of the *LBM* and *BMBL* recommend against the use of ultraviolet light in BSCs.[11,12,137] Experts recommend against the use of UV light as the sole means of decontamination of surfaces within the BSC because efficacy of the method is limited by its inability to penetrate dust or other organic material, requirement for specific environmental conditions (i.e., optimum temperature of 77-80°F and relative humidity above 70%), and association of bulb age with reduced germicidal activity.[155] Despite this, UV light is commonly used to decontaminate the internal surfaces of BSCs in low- and middle-income countries where access to and/or funds for chemical disinfectants may be limited. Thus, data are needed to inform the safe and efficacious use of UV light for decontamination of BSCs in regions where chemical disinfectants are not readily available. Some studies have been conducted to assess the efficacy of UV decontamination of BSC surfaces.[156] However, additional data is needed to inform the development of evidence-based protocols for UV decontamination of the BSC. Similarly, BSC manufacturers have recommended that UV bulbs be changed after 6,000 hours of use, but it is unclear if this recommendation is based on scientific evidence.[157] Thus, there is a need to assess the ability of UV light to decontaminate surfaces within the BSC over the life of the bulb. Experiments should be conducted using a variety of biological agents (e.g., bacteria, viruses, fungi, spores, etc.) to ensure that data is available to develop protocols for each agent type. Once appropriate parameters for effective UV decontamination of BSCs have been developed and validated, they should be tested in real world settings to identify human factors (e.g., failure to turn on UV lamps, failure to clean UV bulbs, etc.) that may impact efficacy of the decontamination protocol. Similar experiments could also be performed on other containment devices that utilize UV light for decontamination (e.g., pass-thru boxes, etc.)

Table 77. Notional Research Design for Parameters for UV Decontamination of BSCs and Efficacy of UV Decontamination of BSCs Over the Lifespan of the UV Bulb	
Research Goal	To generate data on parameters for effective UV decontamination of BSCs and efficacy of UV decontamination of BSCs over the lifespan of the UV bulb's lifespan
Key Variables	• Type (e.g., bacteria, virus, fungi, spore, etc.), characteristics (e.g., presence of viral envelope or bacterial capsule, Gram stain reaction, etc.), concentration, and presentation (e.g., wet, dry, etc.) of biological agents used in BSC • Location of microbial organism in the BSC • BSC class/type and size (e.g., four-foot length, six-foot length, etc.) • UV bulb age (e.g., hours used), quality, use frequency (e.g., daily, weekly, etc.), and cleanliness • UV treatment time (e.g., 15 minutes, 30 minutes, one hour, etc.)
Example Protocol	1. Install new UV bulb in accordance with BSC manufacturer recommendations. 2. Place agar plates inoculated with a known concentration of bacteria in selected positions in the BSC (e.g., one placed in each corner and one in the center, etc.). 3. Expose BSC and agar plates to UV light for the selected treatment time. 4. After treatment time has elapsed, incubate plates for an acceptable amount of time at a temperature appropriate to for the biological agent. After incubation, count bacterial colonies

Table 77. Notional Research Design for Parameters for UV Decontamination of BSCs and Efficacy of UV Decontamination of BSCs Over the Lifespan of the UV Bulb	
	present to determine efficacy of UV decontamination. If colonies are obvious, repeat experiment with a longer treatment time until all bacteria are killed. 5. Use data to develop a protocol for UV decontamination of BSC after use with the selected biological agent. Validate protocol by repeating a sufficient number of times. 6. To test efficacy of UV decontamination over the lifespan of the UV bulb, install a new UV bulb and run continuously or for a set amount of time each day. 7. At selected intervals (e.g., every 500 hundred or 1,000 hours), perform the validated protocol developed earlier to assess the UV light's ability to decontaminate the samples after the elapsed number of use hours. 8. Continue testing until the UV light fails to kill the selected biological agent. 9. Repeat a sufficient number of times to inform the recommendation of an evidence-based UV bulb replacement schedule.
Experimental Outputs	Validated protocol for UV decontamination of BSC after use with a given biological agent; evidence-based recommendation for UV bulb replacement schedule
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Held K. (2020) BSC MythBusters: Can I Use UV or Any Chemicals as a Disinfectant in my BSC? Prepared for The Baker Company. Available from: https://bakerco.com/wp-content/uploads/2020/03/Can-I-use-UV-or-any-chemical-as-a-disinfectant-in-my-BSC.pdf.

8.2.5 Determination of appropriate use cases for class I BSCs

Class II BSCs are designed to provide protection for the user, the environment, and products handled inside the cabinet when properly maintained and operating as intended, while class I BSCs offer protection for only the user and the environment.[158] As a result, class II BSCs are frequently selected for microbiological laboratories where product protection is a priority. However, in certain contexts, such as low resource settings, class I BSCs may be appropriate due to their lower purchase cost and simpler, less expensive maintenance requirements. Despite the absence of product protection, Class I BSCs should always maintain operator and environmental protection when operating due to the one-way flow of air. Thus, studies are needed to determine if class I BSCs provide the same level of user and environmental protection as class II BSCs, to compare long-term maintenance costs, and assess whether the economic benefits justify selection over cabinets that provide product protection.

Table 78. Notional Research Design for Determination of Appropriate Use Cases for Class I BSCs	
Research Goal	To generate data on the user/environmental protection and product protection offered by class I BSCs, and to determine the costs associated with maintenance of class I BSCs
Key Variables	• Class I BSC brand • Number of replicates/number of BSCs • Method used for user/environmental and product protection testing (e.g., potassium iodide or bacterial challenge) in accordance with applicable standard (e.g., NSF/ANSI 49, BS EN 12469, etc.) • Methods used for annual certification testing (e.g., inflow velocity determined using DIM vs. thermal anemometer, etc.) in accordance with applicable standard • Competency of individual conducting BSC testing and annual certification • Calibration of instruments used for testing and certification in accordance with applicable standard • Testing timeline (i.e., time between repeat testing and total length of study)

Table 78. Notional Research Design for Determination of Appropriate Use Cases for Class I BSCs	
Example Protocol	1. Have a competent BSC technician certify each class I BSC in the study initially and on an annual basis throughout the study period. 2. Have a competent individual perform microbiological and/or chemical tests to determine user/environmental and product protection provided by each BSC in the study. Compare the results of this testing with those typical of class II BSCs to determine if the protection provided by class II cabinets is greater than that provided by class I cabinets. 3. Repeat user/environmental and product protection testing on the selected schedule (e.g., every six months or annually) over the life of the project to determine if the level of protection changes as the BSC ages. 4. Over the life of the project, collect all receipts/invoices for BSC costs (e.g., certifications, maintenance, parts, etc.). Compare the total costs over the project period to those typical of class II BSCs. 5. Use data to determine the level of user/environmental and product protection offered by class I BSCs and the total cost of class I BSC maintenance over the study period.
Experimental Outputs	Evidence-based use cases for class I BSCs

8.2.6 Reliability of steam autoclaves

Current editions of the *BMBL* and the *LBM* both recommend that all labs that utilize infectious materials have access to a method for decontaminating laboratory waste, such as an autoclave; however, these resources specifically recommend the use of pass-through or double-door steam autoclaves in maximum-containment laboratories (i.e., BSL4, ABSL4, and ABSL-4Ag).[11,12] Despite this recommendation, pass-through autoclaves have become a popular choice for installation in lower-level laboratories (e.g., BSL3/ABSL3, BSL2/ABSL2, etc.) as well.[159-161] Unfortunately, the project team's real-world experience, and that of workshop participants, is that pass-through autoclaves experience mechanical issues more often than single-door autoclaves and/or that they take longer to repair, which can result in the unanticipated transport or long-term storage of biohazardous waste. As a result, whether to implement use of a pass-through autoclave in a lower containment laboratory may be a more complex cost-benefit question than it appears. For this reason, there is a need for data regarding the reliability of different types of autoclaves to inform equipment selection during the laboratory design phase. This study should compare the frequency of mechanical failures, the causes of these failures, and the time needed for repair of pass-through and single-door autoclaves. Many institutions likely already have data related to the reliability and maintenance needs of their autoclaves that could be collected and analyzed to provide a starting point for this study.

Table 79. Notional Research Design for Reliability of Steam Autoclaves	
Research Goal	To generate data on the reliability and anticipated maintenance needs of autoclaves to inform the selection of autoclaves during the laboratory design phase
Key Variables	• Autoclave type (e.g., pass-through or single door) and brand • Autoclave size/volume • Water quality • Frequency of autoclave use and common load types (e.g., solids/liquids, high temperature, long treatment time, etc.) • Commonly used autoclave cycle types (i.e., gravity, vacuum, or liquid) and cycle parameters (i.e., time, temperature, and pressure) • Frequency and quality of preventative maintenance service

Table 79. Notional Research Design for Reliability of Steam Autoclaves	
	• Types of mechanical failures (e.g., gasket failure, valve failure, heating element failure, pressurization issues, etc.) • Study length (e.g., one year, five years, etc.)
Example Protocol	1. Identify a cohort of laboratories that use autoclaves of different types, brands, sizes, ages, and with different use and maintenance profiles. 2. Survey selected laboratories about the frequency of mechanical autoclave failures, the causes of failures, and the length of time required for repairs. 3. Compare survey data for different types of autoclaves to determine autoclave type that is most reliable over time.
Experimental Outputs	Autoclave type that is most reliable over time

8.3 Data Needs for Application of Primary Containment Devices

8.3.1 Determination of laboratory procedures that require primary containment

Studies have demonstrated that infectious aerosols and/or airborne droplets are often generated during common laboratory procedures.[31-33] Laboratories have implemented safety measures (e.g., use of BSCs, inward airflow and HEPA filtration of exhaust in laboratories, etc.) to contain the aerosols generated during lab work; however, the aerosols produced during many common laboratory procedures have not been fully characterized and it is unclear whether primary containment is needed.[162] Researchers have quantified and characterized the aerosols produced during some laboratory procedures, such as homogenization, vortexing, pipetting, serial dilution, and centrifugation, but there is a need for additional reps of these experiments, as well as characterization of other laboratory procedures.[31-33] If respirable aerosols are generated by a specific procedure, experiments should be conducted to determine the efficacy of primary containment devices in containing the aerosols. Aerosol quantification and characterization experiments should be carried out for a variety of different laboratory procedures with various pathogen types (e.g., bacteria, viruses, fungi, etc.).

Table 80. Notional Research Design for Determination of Laboratory Procedures that Require Primary Containment	
Research Goal	To generate data on aerosols generated during laboratory procedures and the containment measures needed
Key Variables	• Laboratory procedure • Biological agent/surrogate type and concentration • HVAC parameters • Aerosol sampling device (e.g., particle counter/sizer, cyclone sampler, slit sampler, Andersen sampler, etc.) and operation parameters (e.g., placement, volume of air sampled, operation time, etc.) • Primary containment method (e.g., use of gasketed tubes in centrifugation, completion of procedure in BSC, placement of equipment, etc.) • Total sampling time (e.g., 30 minutes, 60 minutes, etc.)
Example Protocol	1. Perform laboratory procedure without primary containment measures while using selected sampling device(s) to determine if aerosols are generated and, if so, to measure the total number of particles generated and the size distribution of the microbial aerosol. 2. If aerosols are generated, repeat procedure with primary containment measures in place to ensure that these measures prevent the escape of aerosols during the procedure.

Table 80. Notional Research Design for Determination of Laboratory Procedures that Require Primary Containment	
	3. Repeat procedure a sufficient number of times to generate sufficient data to develop an evidence-based recommendation for the primary containment measures needed for a given laboratory procedure.
Experimental Outputs	Rates and types of contamination produced during common laboratory practices; evidence-based recommendations for laboratory procedures that require primary containment
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Gassiep I et al. (2021) Laboratory safety: handling Burkholderia pseudomallei isolates without a biosafety cabinet. *J Clin Microbiol*. 59 (7): e0042421. • Miller HE et al. (2014) Characterization of respirable aerosols generated during routine laboratory procedures. *Appl Biosaf.* 19 (1)**:** 19-27. • Pottage T et al. (2014) Quantification of microbial aerosol generation during standard laboratory procedures. *Appl Biosaf.* 19 (3)**:** 124-131. • Pottage T et al. (2022) Microbial aerosols generated from standard microbiological laboratory procedures. *Appl Biosaf.* 27 (2)**:** 92-99.

9 Research Opportunities Related to Verification and Certification

9.1 Data Needs Related to Facility Verification

9.1.1. Verification frequency of high- and maximum-containment laboratories

Current guidance recommends annual verification of HVAC and facility design and operational parameters for high- and maximum-containment laboratories.[11,12,144] This verification process may include, but is not limited to, the following:

- Confirmation that the primary means of detecting facility airflow (e.g., magnehelic gauge, etc.) measures and displays the flow of air as measured and are calibrated, as required;
- Confirmation that airflow into the laboratory is inward/directional without reversal during failure conditions (e.g., transition from normal to backup power sources during power failure, supply fan failure, exhaust fan failure, etc.);
- Confirmation that systems used for the decontamination of biohazardous wastes (e.g., autoclaves, incinerators, tissue digestors, effluent decontamination systems, etc.) are operating correctly;
- Confirmation that facility operation systems (e.g., building automation systems [BAS], etc.) are functioning properly and monitoring/recording performance measurements as intended;
- Confirmation that installed safety alarms (e.g., airflow alarms, fire alarms, security alarms, etc.) are functioning as intended;
- Certification of HEPA filters installed in the facility HVAC system, if applicable;
- Maintenance of exhaust fan motors;
- Repair of penetrations, cracks, and/or breaks in laboratory surfaces; and
- Confirmation that safety showers, eye washes, and hands-free sinks are operating as intended;
- Confirmation that containment systems (e.g., door gaskets, HVAC dampers, airlocks, interlocks, etc.) are functioning as intended.[163,164]

This verification process provides assurance that containment facilities are operating as designed; however, the process is time consuming, expensive, utilizes specialized equipment, and requires expertise (e.g., licensing to test and certify HEPA filters, etc.) that may not be available in all locations. Additionally, the requirement for annual verification of these containment facilities does not appear to be based on experimental data. It is possible that facilities could be verified on a less frequent basis and still provide adequate containment. Alternatively, it is also possible that facilities require verification on a more frequent basis to provide adequate protection. Empirical evidence regarding how long HVAC systems and facility design and operational parameters perform as intended under typical facility use conditions is needed to ensure containment of the work conducted in these facilities, and these data may provide justification for an altered laboratory verification schedule. Experiments should be carried out in various types of high- and maximum-containment facilities (e.g., conventional laboratories, insect facilities, animal housing facilities, etc.) to account for the effects of the environment (e.g., presence of animal dander, temperature, relative humidity, etc.) on the facility HVAC system and other operational parameters.

Table 81. Notional Research Design for Required Frequency of Laboratory Verification

Research Goal	To generate data on the appropriate verification cycle for high- and maximum-containment laboratories
Key Variables	• Facility containment level (e.g., CL 3 &4, PC 3 & 4, BSL3 & 4, ABSL3 & 4, etc.) • Facility type, location, internal environmental conditions (e.g., presence of animal dander, etc.) and external environmental conditions (e.g., loadshedding, high temperatures, etc.) • Number of replicates/number of facilities • Testing timeline (e.g., three months, six months, etc.) • Design and operational parameters confirmed, and methods, equipment, and expertise required for each
Example Protocol	1. Install new HEPA filter(s) (if present) and verify facility components in accordance with applicable recommendation or requirement. 2. Re-test each design/operation parameters on a chosen justifiable schedule (e.g., every three or six months) until the given parameter fails testing or reaches the chosen experimental end point.
Experimental Outputs	% of facilities and specific components that fail testing of each given parameter at given timepoints and conditions of failure
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • ANSI, ASSP. (2020) ANSI/ASSP Z9.14 - 2020 Testing and Performance-Verification Methodologies for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Ventilation Systems. Park Ridge, Illinois, USA: ASSP. • Colella J et al. (2013) The endurance testing process: a methodology to verify the functionality of biocontainment, security, and life safety systems in BSL-3 and BSL-4 laboratories. *Appl Biosaf.* 18 (1)**:** 18-23. • Frasier D. Annual Performance Verification for ABSL3 and BLS3 [sic] Facilities. Prepared for Cornerstone Commissioning Services. Available from: https://absaconference.org/wp-content/uploads/2014/06/XVIII-4-Frasier-430.pdf. • Ziegler C, Tremblay, G. (2019) Merrick White Paper: Boundary Integrity Testing of CL3 (BSL3) Biological Containment Laboratories. Prepared for Merrick & Company. Available from: https://www.merrick.com/wp-content/uploads/2020/01/Room-Integrity-Testing.pdf.

9.2 Data Needs Related to Recertification Engineering Controls

9.2.1 Tests needed for recertification of class I and class II BSCs

Current editions of major international standards for BSC performance, such as NSF/ANSI 49 and BS EN 12469, recommend that BSCs undergo field testing on an annual basis to verify that each cabinet continues to meet relevant performance criteria. Tests required to be conducted as part of annual certification in many countries typically include testing of volumetric airflow rates (i.e., downflow velocity testing and/or inflow velocity testing), airflow patterns testing, and filter leak testing. However, these standards also contain parameters for additional microbiological and/or chemical tests designed to demonstrate the cabinet's ability to protect the user, other laboratory personnel, and products handled within it.[136,137] These additional testing methods are not always required, but previous studies have demonstrated that certified BSCs can fail user protection testing for no apparent reason, so it is unclear if the in situ tests used for certification are useful.[165] As such, the use of these additional tests may be more beneficial for annual certification of BSC function as they provide a quantitative measure of the actual protection provided by the cabinet. Thus, there is a need for experiments which compare the results of volumetric airflow testing with those from personnel protection, product protection, and cross-contamination testing to determine if airflow testing is truly indicative of the protection provided by BSCs or if these additional tests should be completed as part of the annual recertification process. Experiments should be carried out with a variety of brands of both class I and class II BSCs, as well as different types of class II BSCs.

Table 82. Notional Research Design for Tests Needed for Recertification of Class I and II BSCs

Research Goal	To generate data comparing the results of recommended BSC field tests with the results of personnel protection, product protection, and cross-contamination testing
Key Variables	• BSC class, type, and brand • Number of replicates/number of BSCs • Certification standard (e.g., NSF/ANSI 49, BS EN 12469, AS 2252.4, GB 50346, etc.) • Competency of BSC certification technician • Methods used for testing (e.g., inflow velocity determined using DIM vs. thermal anemometer, KI-DISCUS vs. microbiological testing, etc.) • Calibration of instruments used for certification testing in accordance with applicable standard • Testing timeline (i.e., time between repeat testing and total length of study)
Example Protocol	1. Identify as many BSCs of different types and conditions as possible for inclusion in the study. 2. For each BSC in the study, perform recommended microbiological and/or chemical tests in accordance with the applicable standard to determine if the cabinets are providing adequate protection. a) Perform the personnel protection test on class I BSCs. b) Perform the personnel protection, product protection, and cross contamination tests on class II BSCs. 3. When microbiological/chemical testing is complete, have a competent BSC technician perform volumetric airflow certification testing in accordance with the applicable standard. 4. Determine how often volumetric airflow testing indicates that a BSC is functioning within acceptable limits when microbiological/chemical testing indicates that the cabinet is not providing the intended level of protection. If this occurs on a regular basis, addition of microbiological/chemical testing to the annual certification testing process should be considered.
Experimental Outputs	Evidence-based certification testing process for class I and II BSCs

Table 82. Notional Research Design for Tests Needed for Recertification of Class I and II BSCs	
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Hinrichs T, Gragert S, Klein M. (2016) Biological safety cabinets: simulation and quantifying of airflow perturbation caused by personnel activities. *Appl Biosaf*. 21 (1): 12-18.

9.2.2 Performance standard for downdraft tables

Downdraft tables are often used to provide primary containment for procedures involving animals that are too large to fit in a BSC. These devices are similar to BSCs in that they minimize exposure of personnel to infectious aerosols by drawing air into the work surface and exhausting it through a HEPA filter.[166] The NIH has developed testing methods and acceptance criteria for downdraft tables, but there are no widely accepted standards for the performance of downdraft tables.[118,167] Thus, studies are needed to identify the downdraft table metrics that should be tested to measure performance, develop testing methodologies for each performance metric, determine acceptance criteria for each test, and establish the frequency with which testing should be conducted. The first step in this process will be to establish a worker protection assay, similar to the personnel protection test described in NSF/ANSI 49 for use with BSCs, for measuring the protection provided by downdraft tables.[137] This assay can then be used in the development of a standard for downdraft table performance.

Table 83. Notional Research Design for Performance Standard for Downdraft Tables	
Research Goal	To generate data to inform the development of standard methods and acceptance criteria for performance testing of downdraft tables
Key Variables	• Downdraft table type and brand • Number of replicates/number of downdraft tables • Potential performance metrics (e.g., airflow rates, airflow patterns, HEPA filter integrity, etc.) • Methods and equipment for testing performance metrics • Required frequency of testing
Example Protocol	1. Develop a worker protection assay for measuring the protection provided by a downdraft table. 2. Use the worker protection assay to test the protection provided by downdraft tables under various perturbations. 3. Determine how those perturbations influence downdraft table performance. 4. Use data to determine different metrics to be included in the standard.
Experimental Outputs	Worker protection assay for use in testing of downdraft tables; standard for downdraft table performance
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • NSF & ANSI. (2022) NSF/ANSI 49-2022 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification. Ann Arbor, Michigan, USA: NSF International. • NIH. (2011) Local Exhaust Ventilation Testing Protocols Prepared for NIH. https://ors.od.nih.gov/sr/dohs/Documents/nih-local-exhaust-ventilation-testing-protocols.pdf.

9.3 Data Needs for the Recertification Frequency of Engineering Controls

9.3.1 Certification frequency of HVAC HEPA filters

There is a need for real-world data regarding how long HVAC HEPA filters retain their efficacy under typical facility conditions. Such data will support safe containment of research conducted in facilities and may provide justification for an altered HEPA filter recertification schedule. Experiments should be carried out in various research facilities (e.g., plant facility or greenhouse, animal research areas, standard lab space, etc.) to account for the impact of the environment (e.g., presence of soil, fungal spores, or animal dander, relative humidity, etc.) on loading of the filter(s).

Table 84. Notional Research Design for HEPA Filter Testing

Research Goal	To generate data on the appropriate recertification cycle for HEPA filters
Key Variables	• HEPA filter type • Facility type/other use parameters • Number of replicates/number of HVAC systems • Testing timeline (e.g., three months, six months, etc.) • Testing method • Environmental factors (e.g., temperature, relative humidity, altitude, etc.) • External factors (e.g., ash from wildfires, etc.)
Example Protocol	1. Install new exhaust HEPA filter(s) and use *in-situ* testing to confirm filter integrity and performance in accordance with ISO 16170:2016 or another applicable standard. 2. Re-confirm filter integrity and performance on a chosen justifiable schedule (e.g., every three or six months) until the filter fails testing or reaches the chosen experimental end point.
Experimental Outputs	% of filters that fail at given timepoints and conditions of failure

9.3.2 Certification frequency of BSCs

Widely accepted standards require certification of BSCs at the time of installation, if the equipment is moved, and annually thereafter; however, this schedule is not based on experimental data.[168] Empirical evidence regarding how long BSCs provide adequate protection under typical facility conditions is needed to ensure the safety of BSC users, and these data may provide justification for an altered BSC recertification schedule. Experiments should be carried out in various types of research facilities (e.g., plant facility or greenhouse, animal research areas, standard lab space, etc.) to account for the effects of the environment (e.g., presence of soil, fungal spores, or animal dander, relative humidity etc.) on loading of the BSC HEPA filter(s). Additionally, typical use parameters of the BSC (e.g., constant running, sporadic use, etc.) should be incorporated into the experiments.

Table 85. Notional Research Design for BSC Recertification

Research Goal	To generate data on the appropriate recertification cycle for BSCs
Key Variables	• BSC class/type • Facility type and BSC use parameters (e.g., routine microbial culturing, lab animal cage changes, etc.) • Number of replicates/number of BSCs • Testing timeline (e.g., three months, six months, etc.) • Certification standard (e.g., NSF 49, EN 12469, etc.)
Example Protocol	1. Install new HEPA filter(s) and certify BSC in accordance with NSF 49 or another applicable standard. 2. Test BSC on a chosen justifiable schedule (e.g., every three or six months) until the cabinet fails testing or reaches the chosen experimental end point.

Table 85. Notional Research Design for BSC Recertification	
Experimental Outputs	% of filters that fail at given timepoints and conditions of failure

9.3.3 Certification frequency of actively ventilated isolator caging systems

There is a need for experimental data regarding how long HEPA filters used in actively ventilated isolator caging systems retain their integrity under typical use conditions. These data will ensure safe containment of animals infected with biological agents and may provide justification for an altered recertification schedule for caging systems. Experiments should be carried out with various lab animal species (e.g., mice, rats, Guinea pigs, etc.) and bedding types (e.g., wood chips or shavings, cob, cotton nesting, etc.) to account for their impacts on loading of the HEPA filter(s). Typical use parameters of the caging system (e.g., constant running, sporadic use, etc.) should be incorporated into the experiments as well.

Table 86. Notional Research Design for Caging System Recertification	
Research Goal	To generate data on the appropriate recertification cycle for actively ventilated isolator caging systems
Key Variables	• Caging system use parameters (e.g., animal species, bedding type, etc.) • Number of replicates/number of caging systems • Testing timeline (e.g., three months, six months, etc.) • Certification method
Example Protocol	1. Install new HEPA filter(s) and certify in accordance with manufacturer instructions. 2. Recertify on a chosen justifiable schedule (e.g., every three or six months) until the filter fails testing or reaches the chosen experimental end point.
Experimental Outputs	% of filters that fail at given timepoints and conditions of failure

9.4 Data Needs for the In-House Verification of Facility Equipment

9.4.1 Verification frequency of autoclaves and reasons for failure

The current edition of the *LBM* advises development of a process that routinely verifies that an autoclave is functioning correctly via the use of appropriate biological indicators (BIs) such as those containing *Geobacillus stearothermophilus.*[12] The CDC recommends daily or weekly BI verification of autoclaves used in healthcare or dental facilities; however, there is no recommended verification schedule for autoclaves that are used to treat waste in research facilities.[83,169] Many research institutions perform monthly autoclave verifications using BIs, but this frequency appears to be arbitrary.[170,171] There is a need for real-world data regarding the frequency with which an autoclave fails to decontaminate a given load type. These data will ensure that biohazardous waste is decontaminated during autoclaving and may provide justification for an altered autoclave verification schedule. There is also a need for data regarding the causes of autoclave failures (e.g., loss of pressure, inconsistent heating, low humidity, etc.). Determining the causes of autoclave cycle failure will require the inclusion of probes or sensors which can provide real-time measurements of various autoclave cycle parameters. Experiments should be carried out with various load types (e.g., lab

disposables/used PPE, used growth medium, soil, animal carcasses, etc.) to account for the impacts a load type may have on successful decontamination.

Table 87. Notional Research Design for Verification Frequency of Autoclaves and Reasons for Failure

Research Goal	To generate data on the rates and causes of autoclave cycle failure to inform the frequency of in-house verification
Key Variables	• Autoclave parameters (e.g., time, temperature, and pressure) • Probe/sensor type (e.g., temperature, pressure, humidity, etc.) and placement • BI type and placement • Load type (e.g., lab disposables, liquids, soil, carcasses, etc.) and arrangement
Example Protocol	1. Place waste load, BIs, and probes/sensors in chosen arrangement in autoclave and run cycle using chosen parameters. Incubate BIs in accordance with manufacturer instructions to assess decontamination. 2. If autoclave cycle fails, use probe/sensor data to determine the reason for failure of the cycle and perform maintenance/repairs if needed. 3. Re-confirm decontamination on the chosen schedule (e.g., daily, weekly, etc.) until the chosen experimental endpoint is reached.
Experimental Outputs	% of autoclave cycles that fail and conditions of failure; evidence-based autoclave verification frequency

Data Needs and Notional Study Designs for Biorisk Management Systems and Personnel

10. Research Opportunities Related to Biorisk Management Systems

10.1 Data Needs for Biorisk Management Program Leadership

10.1.1 Optimal leadership structure to support biorisk management system implementation

The International Organization for Standardization (ISO) 35001 Biorisk Management for Laboratories and Other Related Organisations standard states that management within an institution has overall responsibility for biorisk management system implementation and must support this implementation by providing adequate resources (e.g., personnel, facilities, etc.), promoting the system to applicable institutional personnel, and establishing procedures to ensure that the system is operating effectively.[172] However, the standard does not specify a leadership structure that supports implementation of a biorisk management system in an optimal way. A 2019 survey of over 150 Institutional Biosafety Committee (IBC) contacts and Biosafety Officers (BSOs), mainly from academic institutions, revealed that the majority (45%) of IBCs at surveyed institutions report to a Vice President or Chancellor for Research, while 60% of BSOs from those same institutions report to the head of Environmental Health and Safety (EHS).[173] Despite these being the most common leadership structures for the institutions surveyed, it is unclear whether these structures support biorisk management implementation and, if so, why they are beneficial. As such, there is a need for data regarding the impact of management structure on implementation of a biorisk management system within an institution to determine which structure(s) and associated characteristics are most advantageous.

Table 88. Notional Research Design for Leadership Structure to Support Biorisk Management System Implementation

Research Goal	To generate data on the impact of different leadership structures on biorisk management system implementation
Key Variables	• Leadership structure for IBC and BSO (e.g., reporting to Vice President/Chancellor for Research, EHS, Research Integrity/Compliance, Sponsored Programs, President/CEO, and all possible combinations) • Biorisk management program scope (e.g., use of animals, plants, or arthropods with biohazardous materials, use of biological toxins, use of bloodborne pathogens [BBP], use of recombinant or synthetic nucleic acids [r(s)NA], use of nanomaterials, etc.) • Biorisk management program size (i.e., number and types of researchers, number of laboratories, number of research protocols, etc.) • Biorisk management program complexity (e.g., use of multiple regulated materials [BBP, select agents, r(s)NA], performance of tasks related to biosafety [e.g., applying for and maintaining federal permits, occupational health, biorisk management committee support, laboratory decontamination, etc.])
Example Protocol	1. Design a survey to collect information from biosafety personnel about the type of leadership structure at their institution (e.g., positions, reporting lines, organizational charts, leadership style, etc.), operational characteristics of this structure (e.g., decisions left to biosafety personnel vs. leadership, how resources are allocated, frequency of communication, escalation processes, etc.), culture (e.g., trust in leadership, staff satisfaction, empowerment of biosafety

Table 88. Notional Research Design for Leadership Structure to Support Biorisk Management System Implementation	
	personnel, etc.), and program effectiveness (e.g., components and processes that support versus hinder biorisk management implementation). 2. Identify a large cohort of institutions with biorisk management systems of different scopes/sizes/risk profiles and various leadership structures to complete the survey. 3. Design a separate survey to collect information from the leaders that biosafety personnel report to regarding their viewpoints on the type of leadership structure at the institution (e.g., leaders' background and leadership style, positions, reporting lines, organizational charts, etc.), operational characteristics of this structure (e.g., decisions left to biosafety personnel vs. leadership, how resources are allocated, frequency of communication, escalation processes, etc.), culture (e.g., trust in leadership, staff satisfaction, empowerment of biosafety personnel, etc.), and program effectiveness (e.g., components and processes that support versus hinder biorisk management implementation). 4. Analyze survey results to compare the perceptions of leadership and biosafety personnel and identify best practices for leadership structures that support successful biorisk management implementation.
Experimental Outputs	Evidence-based recommendations for leadership structures that enable effective implementation of biorisk management systems

10.2 Data Needs for Biorisk Management Program Administration

10.2.1 Determining sufficient staffing levels for biorisk management programs

The ISO 35001 Biorisk Management for Laboratories standard states that the leadership within an institution is responsible for ensuring that the resources needed for the safe operation of the biorisk management system (e.g., appropriate and adequate personnel, facilities, etc.) are available.[172] Unfortunately, there is little guidance related to the proper staffing of biorisk management programs. A 2019 survey of more than 150 IBC contacts and Biosafety Officers found that most of the institutions surveyed had one or fewer IBC support staff and one dedicated biosafety staff (i.e., a Biosafety Officer) for every 125 IBC protocols reviewed. The study also found that institutions that conduct research with select agent organisms and/or house high containment (i.e., BSL3) laboratories have three dedicated biosafety personnel, on average.[173] However, it is likely that the number of personnel needed to run a biorisk management program also depends on additional factors, such as the scope of activities conducted at the institution, the relative size of the program, and the complexity of the program. Thus, there is a need for data regarding the number of personnel required to sufficiently staff a biorisk management program. This information should then be used to develop a matrix to assist institutions in determining the number of dedicated personnel needed to administer a biorisk management program based on its scope, size, and complexity. Additionally, this information will assist institutions in determining appropriate biorisk management program budgets.

Table 89. Notional Research Design for Determining Sufficient Staffing Level for Biorisk Management Programs	
Research Goal	To generate data on the dedicated staff needed to administer a biorisk management program to inform the development of a biorisk management program staffing matrix
Key Variables	• Organizational design (e.g., what biorisk management -related processes [occupational health, general laboratory safety, etc.] belong to which groups [Biorisk Management, Environmental Health & Safety, Chemical Safety, Life Safety, etc.])

Table 89. Notional Research Design for Determining Sufficient Staffing Level for Biorisk Management Programs	
	• Roles and responsibilities of biorisk management program staff (e.g., laboratory inspections, training, biological agent inventory reconciliation, biorisk management committee management, etc.) • Biorisk management program scope (e.g., use of animals, plants, or arthropods with biohazardous materials, use of biological toxins, use of BBPs, use of r(s)NA, use of nanomaterials, etc.) and associated requirements • Biorisk management program size (i.e., number and types of researchers, number of laboratories, number of research protocols, etc.) • Biorisk management program complexity (e.g., use of multiple regulated materials [BBP, select agents, r(s)NA], performance of tasks related to biosafety [e.g., applying for and maintaining federal permits, occupational health, biorisk management committee support, laboratory decontamination, ensuring proper waste management, etc.) • Administrative processes used (e.g., use of protocol management system, methods for tracking laboratory inspections, training, and occupational health program enrollment, etc.) • Role of biorisk management committee members (e.g., Do members only perform committee duties or do they assist with other tasks that may typically be performed by biorisk management program staff?) • Method for determining program efficacy (e.g., staff perceptions of efficacy, etc.)
Example Protocol	1. Design a survey to collect information related to biorisk management program scope, size, complexity, administrative processes, efficacy, staffing, the role of biorisk management committee members, and if staff believe biorisk management staffing is sufficient. 2. Identify a cohort of biorisk management program personnel from various types of institutions (e.g., academic, clinical, industry, etc.) to complete the survey. 3. For each institution in the cohort, curate additional data that may indicate the sufficiency of staffing (e.g., how often do tasks go uncompleted, how often do staff work overtime, etc.). 4. Aggregate data for biorisk management programs that are deemed to have a sufficient staffing level based on the selected method and determine the number of personnel required based on program scope, size, and complexity. 5. Use resulting data to develop a staffing matrix for biorisk management programs.
Experimental Outputs	Evidence-based matrix to assist institutions in determining the number of dedicated personnel needed to administer a biorisk management program based on its scope, size, and complexity
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Johnson CM, Dobos KM. (2019) The evolving landscape of institutional biosafety committees and biosafety programs: results from a national survey on organizational structure, resources, and practices. *Appl Biosaf*. 24 (4): 213-219.

10.2.2 Adequate funding of biorisk management programs

The current edition of the *LBM* states that the responsibility for providing adequate funding to a biorisk management program lies with institutional management.[12] This funding is needed for human resources (e.g., biosafety personnel, biorisk management committee personnel, etc.), infrastructure, and implementation of program processes (e.g., risk assessment, research protocol review, laboratory inspections, etc.); however, there is a lack of guidance regarding what an appropriate institutional budget for a biorisk management program should include.[174] Thus, there is a need for real world data to inform the items that should be included in the budget of an effective biorisk management program. Analyses performed to obtain data related to this need should consider biorisk management programs of different scopes (e.g., types of activities conducted with

biohazardous material), sizes (e.g., numbers of biorisk management personnel, principal investigators, research personnel, laboratories, etc.), different complexities (e.g., low- versus high-containment level laboratories, use of regulated materials, use of animals or invertebrates, aerosolization studies, etc.), and the various components of the biorisk management program (e.g., biorisk management committee coordination, laboratory decontamination processes, laboratory inspections, occupational health, etc.) and the needs associated with each (e.g., computer equipment, computer software, laboratory decontamination equipment, consumables, etc.). Additionally, analyses should consider routine costs (e.g., annual verification of high- and maximum-containment laboratories) as well as those that occur on a less common basis (e.g., new computer equipment every three years).

Table 90. Notional Research Design for Adequate Funding for Biorisk Management Programs

Research Goal	To generate data on the items that should be included in the budget of a biorisk management program
Key Variables	• Organizational design (e.g., what biorisk management -related processes [occupational health, general laboratory safety, etc.] belong to which groups [Biorisk Management, Environmental Health & Safety, Chemical Safety, Life Safety, etc.] • Biorisk management program scope (e.g., use of animals, plants, or arthropods with biohazardous materials, use of biological toxins, use of BBPs, use of r(s)NA, use of nanomaterials, etc.) and associated requirements (e.g., expertise needed for protocol review, required frequency of inspections, meeting frequency, need for occupational health services, etc.) • Administrative processes used (e.g., use of protocol management system, methods for tracking laboratory inspections, training, and occupational health program enrollment, etc. • Human resource costs (e.g., staff salaries, training costs, service engineers for equipment and facility, laboratory certifiers and auditors, etc.) • Administrative needs (e.g., computer equipment and supplies, protocol management software, biorisk management committee support, etc.) • Miscellaneous expenses (e.g., spare parts for laboratory equipment [e.g., autoclave, BSC, centrifuge, effluent decontamination system, animal cages/racks, autopsy table, tissue digester, etc.], facility project management services [e.g., building management system, security system, ventilation system, etc.], consumables and laboratory operations [e.g., utilities, housekeeping, laundry, waste management and disposal, sample/pathogen packaging and transportation, etc.]) • Biorisk Management program components (e.g., occupational health, respiratory protection, laboratory decontamination, etc.) • Costs associated with management of the biorisk management committee (e.g., annual stipends for members, meeting refreshments, computer equipment, etc.) • Budget period (e.g., one year, three years, five years, etc.)
Example Protocol	1. Design a survey to collect information about the items included in the budgets of biorisk management programs. For each biorisk management program component, the survey should collect the specific items included in the budget, with what frequency (e.g., monthly, annually, every other year, etc.) the funds are spent over the budget period, and if the biorisk management personnel being surveyed believe the funding is adequate for that component. 2. Identify a cohort of effective biorisk management programs from institutions with different profiles located in different countries/regions to complete the survey. 3. Aggregate data from all surveys to determine the items included in the budget for a specific biorisk management program component.

Table 90. Notional Research Design for Adequate Funding for Biorisk Management Programs	
Experimental Outputs	Evidence-based list of items for inclusion in the budget of a biorisk management program based on its scope, administrative needs, and components

10.3 Data Needs for Biorisk Management Committees

10.3.1 Incentive programs to enhance recruitment and retention of high-quality biorisk management committee members

Biorisk management recommendations often call for the establishment of a biorisk management committee (also known as an IBC or Biosafety Committee) to support an entity's biorisk management system.[172] Similarly, some guidelines for handling of specific biological materials require the formation of such a committee charged with the review and approval of research activities involving certain types of regulated materials.[175,176] In either case, these committees are often tasked with a variety of responsibilities including developing policies related to biorisk management, carrying out risk assessments, review and approval of protocols for research involving biological agents, and overseeing the investigation of incidents involving biohazardous materials.[177] Due to the importance of these committees, high-quality members must have specific qualifications and expertise such as experience working with biological agents and/or other regulated materials, an understanding of biosafety and biosecurity practices, and the ability to recognize potential risks in the protocols being reviewed.[178] However, the real-world experience of practitioners in the field is that desirable committee members, those who possess the necessary expertise and are willing to serve on the committee, are often difficult to recruit and retain. As such, there is a need for studies that determine if incentive programs aid in the recruitment and retention of desirable committee members and, if so, what incentives are most effective for this purpose.

Table 91. Notional Research Design for Incentive Programs to Enhance Recruitment and Retention of High-Quality Biorisk Management Committee Members	
Research Goal	To generate data to inform the development of incentive programs to enhance recruitment and retention of desirable biorisk management committee members
Key Variables	• Institutional profile (e.g., number of researchers and/or laboratories, biosafety level of laboratories, use of regulated materials, etc.) • Size of committee/number of committee members • Committee responsibilities and amount of time spent on each • Desired expertise • Training offered • Requirement for inclusion of community members on committee • Length of committee membership term • Incentives offered (e.g., monetary compensation/bonuses, service credits, recognition awards, greater access to leadership, etc.)
Example Protocol	1. Identify two cohorts of research subjects from multiple institutions with different profiles: a) High-quality biorisk management committee members (retention group) b) Non-members with desired expertise (recruitment group) 2. Design a survey to collect data from each cohort regarding the incentive(s) that would motivate these high-quality individuals to join or remain on the biorisk management committee.

Table 91. Notional Research Design for Incentive Programs to Enhance Recruitment and Retention of High-Quality Biorisk Management Committee Members	
	3. Using data from the survey, determine the types of incentives to evaluate for each cohort. Divide individuals into the number of groups needed and provide each group with the selected incentive for a chosen period. 4. At selected times throughout the study, survey participants to evaluate attitudes regarding each incentive and whether its implementation motivated individuals to join or remain on the committee. At the same time, survey personnel who manage each committee to evaluate whether implementation of incentives has impacted the quality of committee members. 5. At the end of the chosen period, aggregate survey results to assess which incentives correlated with enhanced recruitment and retention of high-quality committee members. 6. Repeat implementation of the top performing incentives with a new set of returning and prospective committee members to determine effects in new/additional institutions.
Experimental Outputs	Incentive program to enhance recruitment and retention of high-quality biorisk management committee members
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Jessani NS et al. (2020) Academic incentives for enhancing faculty engagement with decision-makers—considerations and recommendations from one School of Public Health. *Humanit Soc Sci Commun*. 7 (1): 148.

10.3.2 Guidelines for biorisk management committee protocol review processes

As mentioned above, standards, guidelines, and regulations related to biorisk management often recommend or require the formation of biorisk management committees to review and approve protocols for research involving biohazardous materials.[12,175,179] The U.S. NIH's *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines*) state that reviews conducted by an IBC should include an assessment of the proposed containment level for the research, evaluation of the facilities in which the research will be carried out, examination of the practices and procedures to be used during the research study to ensure safety, and review of the training and competence of research personnel involved in the study.[175] Unfortunately, there is a lack of resources that describe how these evaluations should be conducted or what committee members should look for when conducting the evaluations. As a result, individual committees have developed their own review processes; however, the use of these ad hoc processes is likely to result in some biorisk management committees not considering specific items that are beneficial when included in the review processes of other biorisk management committees. Thus, there is a need for studies which compare the protocol review processes of a variety of biorisk management committees to develop guidelines that outline how research protocols should be reviewed and what specific items should be considered during each review.

Table 92. Notional Research Design for Biorisk Management Committee Protocol Review Processes	
Research Goal	To generate data on the review processes of various biorisk management committees to develop guidelines for the review of research protocols involving the use of biohazardous materials
Key Variables	• Number of biorisk management committees and makeup of each committee (e.g., number of members, member experience and expertise, etc.) • Types of research typically reviewed by each biorisk management committee (e.g., high- and maximum-containment containment studies, use of animal/plant hosts, recombinant/synthetic nucleic acids, etc.)

Table 92. Notional Research Design for Biorisk Management Committee Protocol Review Processes	
	• Information collected during protocol submission (e.g., biological agents to be used, activities conducted with biological agents, research facility details, training and experience of research personnel, proposed safety measures, treatment and disposal of biohazardous wastes, etc.) • Regulations applicable to biorisk management committee and/or proposed research study • Method of protocol review (e.g., full committee vs. designated member review vs. Biorisk Management Officer review, etc.) • Length of protocol approval and inclusion of renewal processes
Example Protocol	1. Identify a cohort of biorisk management committees that have similar levels of expertise, oversee similar types of research, adhere to the same applicable regulation(s), and are willing to take part in the study. 2. Develop a research protocol that includes a variety of materials and/or practices that would typically garner committee discussion (e.g., use of risk group 3 and/or 4 agents, aerosolization of agents outside of primary containment, infection of animals, use of sharps, inclusion of personnel with very little experience, proposed use of inadequate laboratory space, etc.) and submit for review by each committee. 3. Observe the process that each committee follows when reviewing the protocol. Take note of each item that is discussed/considered, the order in which they are discussed/considered, and the important factors for each item. 4. Once all committees have reviewed the protocol, aggregate the data to develop a proposed process for the review of research protocols by biorisk management committees. This process should include the items to be considered, the order in which those items should be considered (if relevant), and the important factors for each item. 5. Provide the proposed process to each of the committees for comment and revise as necessary. 6. Provide the completed process to additional biorisk management committees for use. 7. Survey members of these additional committees regarding applicability of the process, if its use was helpful when reviewing research protocols, and any revisions needed. 8. Finalize the protocol review process and make widely available for biorisk management committee use.
Experimental Outputs	Evidence-based process for review of research protocols by biorisk management committees

10.4 Data Needs for Performance and Evaluation/Inspections and Audits

10.4.1 Frequency of laboratory inspections

A laboratory inspection is an observation of the condition of a laboratory at a specific moment in time, while an audit involves an exhaustive review of the biorisk management program for a laboratory or institution. An inspection is typically short and only identifies obvious deficiencies, while an audit takes place over a longer period, allowing for a detailed review of a program and investigation into any identified deficiencies.[180] Audits are generally conducted less frequently than inspections and are intended to assess compliance with institutional policies and/or applicable regulations.[181] CWA 15793 recommends that organizations conduct inspections and audits at "planned intervals."[179] There is no recommendation for precisely how often audits should be conducted, but some U.S. regulations recommend annual inspection of regulated laboratories. However, it is unclear upon what evidence this recommendation for annual laboratory inspections is based. Thus, there is a need for real-world data regarding how often serious deficiencies (i.e., those deficiencies that impact safety, security, and/or regulatory compliance) are observed during

laboratory inspections and/or audits to inform an evidence-based recommendation for the required frequency of these activities. Studies conducted to generate this data should include a variety of different laboratory/facility types from different institutions with various biorisk management program sizes and/or complexities.

Table 93. Notional Research Design for Frequency of Laboratory Inspections

Research Goal	To generate data on rates of significant deficiencies identified during laboratory inspections or to inform an evidence-based laboratory inspection schedule
Key Variables	• Laboratory biosafety level (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) and associated practices/procedures, safety equipment, and facilities • Biorisk management program size (e.g., number of personnel, number of laboratories/facilities, etc.) and complexity (e.g., broad range of biosafety levels, adherence to multiple regulations, etc.) • Inspection process and procedures (e.g., use of checklists, size and makeup of team, length of process, etc.) • Training and experience of inspectors • Selected inspection timeline (e.g., three months, six months, one year, etc.) • Severity of deficiencies (e.g., minor nonconformities vs. major issues) and frequency of repeat observations • Number of deficiencies recorded during each inspection • Time to closeout of inspection deficiencies • Study length (e.g., three years, five years, etc.)
Example Protocol	1. Identify a cohort of institutions/laboratories for inclusion in the program and assemble a team of inspectors to carry out the study. 2. Review the scientific literature, biorisk management guidelines/recommendations, and relevant regulatory documents to determine the process and procedures to be used during laboratory inspections. 3. Assess the items observed/reviewed during the inspection process and categorize them to determine those deficiencies that would be considered significant. 4. Perform laboratory inspections at various intervals across the cohort (i.e., some labs inspected every 3 months while others are inspected every 6 months). 5. After each inspection, determine the number of significant deficiencies observed. 6. Use the data generated to develop an evidence-based recommendation for the frequency of laboratory inspections that will allow for identification of most significant deficiencies in a timely manner.
Experimental Outputs	Rates of identification of significant deficiencies during laboratory inspections; Evidence-based laboratory inspection frequency
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Rebar R. (2002) The art of biosafety auditing in industry. *Appl Biosaf.* 7 (3)**:** 144-155. • U.S. Centers for Disease Control and Prevention (CDC), U.S. Department of Agriculture (USDA). (2023) Federal Select Agent Program - Inspection Checklists. Available from: https://www.selectagents.gov/compliance/preparing.htm. Last Updated October 31, 2023. Accessed October 19, 2024.

10.4.2 Efficacy of announced and unannounced laboratory inspections

Laboratory inspections are often performed as a means of evaluating the performance of the biorisk control measures implemented in a specific laboratory.[182] Traditionally, laboratory inspections conducted by an institution's biorisk management personnel are scheduled with laboratory

leadership in advance; however, it has become more commonplace for biorisk management personnel to conduct these inspections on an unannounced (i.e., surprise) basis.[183] Laboratory inspections scheduled with research personnel in advance allow the laboratory staff to put their best foot forward, but they may not provide inspectors with a realistic view of the typical conditions within the space.[182-184] Unfortunately, there are very few studies comparing the efficacy of announced and unannounced inspections in evaluating and improving biorisk management performance within laboratories. An unpublished study conducted at the University of Kentucky over a four-year period evaluated the outcomes of both announced and unannounced biorisk management inspections. The study found that surprise inspections provided inspectors with a more informed view of the laboratory conditions, leading to an initial increase in cited deficiencies but a subsequent decrease in the number of deficiencies over time. Additionally, the study demonstrated that implementation of unannounced inspections also resulted in a decrease in the number of deficiencies cited during announced inspections.[183] However, there is a need for additional large-scale studies, similar to the University of Kentucky study, that compare the efficacy of announced and unannounced laboratory inspections in improving biorisk management performance within laboratories. Experiments conducted to provide data related to need should be conducted in institutions of different types (e.g., academic, clinical, agricultural, etc.) and sizes, for laboratories of different levels (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.), and over longer periods to determine the true impact of inspection methodology on evaluating biorisk management performance in laboratories.

Table 94. Notional Research Design for Efficacy of Announced and Unannounced Inspections

Research Goal	To generate data on efficacy of announced and unannounced inspections for evaluating and improving biorisk management performance in laboratories
Key Variables	• Institution type (e.g., clinical, academic, agricultural, etc.) • Laboratory biosafety level (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) and associated practices/procedures, safety equipment, and facilities • Selected schedule for announced and unannounced inspections (e.g., annual announced inspection with three [quarterly] unannounced inspection in the interim) • Availability of biorisk management personnel to perform unannounced inspections • Study length (e.g., one year, three years, five years, etc.)
Example Protocol	1. Identify a cohort of institutions/laboratories for inclusion in the study. 2. Develop inspection checklists specific to each biosafety level and inspection type (e.g., the checklists for announced inspections may include items that require questioning of personnel while the checklists for unannounced inspections include visual items only). 3. Identify biorisk management personnel from each institution to serve as inspectors for the study and train them on the procedures and checklists to be used. 4. Conduct announced and unannounced inspections on the selected schedule for the length of the study. 5. At the completion of each inspection, survey laboratory personnel regarding their perception of the biorisk management program and/or staff. 6. When all inspections are complete, aggregate all findings to determine categories of findings (e.g., improper waste disposal, improper/no use of PPE by personnel, BSC not certified, etc.) that are shared among both inspection types and categories of findings that are unique to each inspection type. 7. Compare the finding prevalence for the announced and unannounced inspections for the same laboratory over the study period. 8. Compare survey results to determine if surprise inspections negatively impact researcher perceptions of the biorisk management program and personnel.

Table 94. Notional Research Design for Efficacy of Announced and Unannounced Inspections	
Experimental Outputs	Efficacy of announced and unannounced laboratory inspections for evaluating and enhancing biorisk management performance
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Trucks HM. (2017) An Assessment of the Effectiveness of Unannounced Safety Inspections Versus Announced Inspections in Academic Research Laboratories That Utilize Biological Hazards. MPH Thesis, College of Public Health. Lexington, KY: University of Kentucky. Available from: https://uknowledge.uky.edu/cgi/viewcontent.cgi?article=1176&context=cph_etds.

10.4.3 Composition of biorisk management inspection teams

As mentioned above, laboratory inspections are often performed as a means of evaluating the performance of the biorisk control measures implemented in a specific laboratory.[182] These inspections are often conducted by laboratory personnel, institutional biorisk management personnel, and/or members of the entity's biorisk management committee; however, there are no recommendations for individuals or roles that should be included on a biorisk management inspection team. Thus, there is a need for studies that assess the effectiveness of various biorisk management inspection committee compositions to determine the optimal team makeup for evaluating biorisk management performance in laboratories. This information will also help institutions to determine if appropriate expertise is available in-house or, if not, what expertise they should identify from outside sources before certain studies are approved. Individuals/roles considered for inclusion on these teams may include biorisk management experts, research scientists, security specialists, occupational health practitioners, veterinarians or trained animal handlers, entomologists, and facility managers. Studies conducted to generate the necessary data should consider the specific needs of different laboratory types and biosafety levels. For example, an individual with veterinary or animal handling experience is not necessary for inspection of a standard BSL2 laboratory because animals are not typically handled in these spaces; however, this expertise would be very important during inspection of a BSL3-Ag facility.

Table 95. Notional Research Design for Composition of Biorisk Management Inspection Teams	
Research Goal	To generate data on the optimal composition of biorisk management inspection teams
Key Variables	• Institution type (e.g., clinical, academic, agricultural, etc.) • Laboratory biosafety level (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) and associated practices/procedures, safety equipment, and facilities • Availability of relevant subject matter (e.g., biorisk management, security, information technology, occupational health, infectious disease, etc.) expertise
Example Protocol	1. Identify a cohort of institutions/laboratories for inclusion in the study. This cohort should include laboratories of different types and containment levels. 2. Identify subject matter experts (SMEs) relevant to the different types of laboratories to be inspected. 3. Develop inspection checklists specific to each laboratory type and biosafety level and train all SMEs on the checklists and other procedures to be used during inspections. 4. For each laboratory, generate inspection teams with different combinations of SMEs and have each team inspect the laboratory. 5. When all inspections are complete, compare the findings from all inspections conducted for the same laboratory.

Table 95. Notional Research Design for Composition of Biorisk Management Inspection Teams	
	6. Determine the composition of the team with the greatest number of relevant inspection findings for each laboratory type/level.
Experimental Outputs	Evidence-based composition of biorisk management inspection teams

10.5 Data Needs for Incident Investigation

10.5.1 Evaluation of strategies to improve reporting rates for laboratory incidents and near-misses

Anonymized, nonpunitive critical incident reporting systems (often with penalties for nonreporting) are part of widely accepted standards of practice in healthcare, nuclear power, and chemical industries.[185-188] When laboratory personnel provide prompt and detailed reports of adverse incidents and near-misses, they mitigate immediate risks and provide their institutions with information that can help to reduce future risk.[189] However, staff often neglect to report these events for a variety of reasons, including fear of punishment, lack of time, complexity of the reporting process, and failure to recognize that an incident warrants reporting.[188,190-193] Thus, there is a need to evaluate the incident reporting structures maintained by institutions to ensure that they are perceived by laboratory workers as safe, accessible, and important to use.

Table 96. Notional Research Design for Evaluation of Strategies to Improve Incident and Near-miss Reporting Rates	
Research Goal	To evaluate the efficacy of strategies to improve reporting of laboratory incidents and near-misses
Key Variables	• Incident/near-miss report rates in target lab and comparable control-condition labs • Staff ability to correctly categorize and report reportable incidents/near-misses • Time required to report incidents/near-misses using reporting system • Staff experience • Staff awareness of reporting systems • Staff perceptions of risks and benefits of reporting
Example Protocol	1. Survey personnel, from a set of labs that already have reporting systems, regarding incident/near-miss report rates and staff perceptions of the reporting system. 2. Based on survey results, develop an improved training program to promote the use of the incident/near-miss reporting systems. 3. Randomize labs to complete the improved training program vs. no-treatment control group. 4. After sufficient time to accumulate potential incidents/near-misses has passed: a) Survey lab personnel again to assess change in perceptions of the modified incident/near-miss reporting system. b) Collect incident/near-miss reports submitted during the study period and compare to earlier reports to assess if the modified program improved the quality of submitted reports.
Experimental Outputs	Estimate of changes in lab staff perceptions and incident/near-miss response rates caused by improved training

10.5.2 Understanding the root causes of laboratory incidents

Laboratory incidents continue to occur despite a focus on minimizing their occurrence and reducing the associated negative outcomes. A recent review of laboratory incidents that occurred between 2000 and 2021 concluded that the rate of laboratory accidents can be reduced through the adoption

of evidence-based biosafety measures that address the various causes of those accidents.[194] Thus, there is a need for a long-term study that inventories the wide variety of incidents that can occur in the laboratory, as well as their frequency and proximal causes, to inform the development of biosafety measures and mitigations that prevent the occurrence of such incidents.

Table 97. Notional Research Design for Understanding the Root Causes of Laboratory Incidents	
Research Goal	To generate data on types of incidents that occur in the laboratory, their frequencies, and proximal causes to inform the development of evidence-based biosafety measures
Key Variables	• Procedures, equipment, and instruments used in the laboratory • Personnel-related factors (e.g., training, experience, etc.) • Method for measuring incidents (e.g., fluorescent tracer and UV light, low dilution C-14 and Geiger counter, continuous video monitoring, etc.)
Example Protocol	1. Set up a mock laboratory with the fixtures, equipment, and instruments typically present in a microbiological laboratory with the addition of video cameras intended to record all activities carried out in the laboratory. 2. Employ laboratory personnel with different levels of training and experience. 3. Have personnel perform common laboratory procedures and assays using dummy samples spiked with an exempt dilution of C-14. 4. At the completion of each procedure/assay or before moving to a new laboratory area, have the individual check for personal contamination by sweeping his/her body with a sufficiently sensitive Geiger counter. 5. If contamination occurs, use video recording to determine the proximal cause of the incident. 6. Repeat this process for the life of the study (e.g., one year, etc.).
Experimental Outputs	Inventory of types, frequencies, and causes of incidents that can occur in the microbiological laboratory

10.5.3 Root cause analysis in biorisk management

In risk management, root cause analysis (RCA) is a structured framework that can be used to identify the factors that lead to deficiencies in performance so that strategies can be developed and implemented to reduce the likelihood of event recurrence.[195] Robust RCA is often used to analyze incidents in the aviation and nuclear power industries. Biorisk management guidelines provided by some regulatory bodies recommend the use of RCA for determining the factors that lead to adverse events in laboratories; however, it is unknown to what degree the full RCA process is used by biorisk management professionals as there are very few publications describing use of the practice for investigation of laboratory incidents, implementation of corrective actions, and/or evaluating the performance of biorisk management systems.[196-198] To increase the use of RCA for incident investigations conducted by biorisk management practitioners, there is a need to determine the current state of RCA in biological laboratories followed by pilot implementation of thorough RCA within a cohort of biorisk management programs to develop best practices for RCA in biological laboratories. These best practices can then be made broadly available to assist other biorisk management programs as they implement the use of RCA.

Table 98. Notional Research Design for Root Cause Analysis in Biorisk Management	
Research Goal	To generate data on the current state of RCA in biorisk management programs and pilot RCA within a cohort of biorisk management programs to develop best practices for the use of RCA during investigation of incidents in biological laboratories

Table 98. Notional Research Design for Root Cause Analysis in Biorisk Management	
Key Variables	• Familiarity of biorisk management program personnel with RCA processes • Ability (e.g., time, training, etc.) and willingness of biorisk management personnel to conduct RCA • Frequency, types, and severity of adverse events in the laboratory • Factors contributing to each incident type (i.e., causal factors) • Study length
Example Protocol	1. Perform a review of the literature and conduct interviews with experts performing RCA in other industries to determine the appropriate RCA framework for use in biological incident investigation. 2. Interview biorisk management personnel to determine the current state of RCA among the programs. Questions should be designed to query where respondents' current processes for incident investigation align and diverge with the developed RCA framework as well as barriers to full implementation. 3. Conduct tabletop exercises with mock incident scenarios to refine the framework before deployment to the cohort for use. 4. Select a cohort of biorisk management programs to implement fully-fledged RCA for investigation of laboratory incidents over the selected study period. 5. At the end of the study period, interview personnel from the pilot cohorts regarding which aspects of the RCA program worked. Use data to finalize the RCA framework and develop best practices for the conduct of RCA for investigation of laboratory incidents.
Experimental Outputs	Evidence-based RCA framework and best practices for use in investigation of laboratory incidents

11. Research Opportunities Related to Risk Assessment

11.1 Data Needs for Risk Assessment

11.1.1 Frequency of risk assessment

Biorisk management guidance documents that address the required frequency of the risk assessment process recommend that a given risk assessment be reviewed, or a new assessment be completed, when significant changes (e.g., new biological agents, laboratory modifications, altered staffing, new equipment, etc.) take place, after an incident or emergency occurs, and/or on a periodic (e.g., annual) basis.[179,199] While these resources recommend that periodic reviews occur on an annual basis, it does not appear that this suggested frequency is based on actual evidence. It is possible for the outputs of risk assessments to change on a less frequent basis. Alternatively, it is possible for the output of a risk assessment to change on a more frequent basis. As such, there is a need for real-world data regarding how often risk assessments actually change, outside of planned changed to research or incidents/emergencies, to inform the development of an evidence-based risk assessment review cycle.

Table 99. Notional Research Design for Frequency of Risk Assessment Review	
Research Goal	To generate data on the appropriate review cycle for completed risk assessments

Table 99. Notional Research Design for Frequency of Risk Assessment Review	
Key Variables	• Type and complexity (e.g., multiple and/or high-risk group biological agents, high risk procedures, etc.) of research protocol/activity that the risk assessment covers • Risk assessment methodology • Number of replicates/number of risk assessments • Selected review schedule and project length
Example Protocol	1. Identify a grouping of documented risk assessments that cover a broad range of research types and complexities. a) Note: Throughout the study, remove risk assessments that change due to significant alterations or an incident/emergency from further review. 2. Review each risk assessment on a chosen justifiable schedule (e.g., three months, six months, etc.) until the risk assessment changes to a degree that requires the implementation or removal of mitigations, or the chosen endpoint of the study is reached.
Experimental Outputs	% of risk assessments that change at given time points; evidence-based review cycle for biorisk assessments

11.2 Data Needs Underlying Biological Agent Risk Assessments

11.2.1 Stability of biological agents in various matrices

The risk associated with a biological agent is based on its hazardous characteristics, such as its infectiousness, host range, route of transmission, and environmental stability. The current edition of the *BMBL* provides high-level stability information for many pathogens; however, this information is still lacking for many organisms.[11] Real-world data regarding the stability of biological agents in or on various matrices are needed for use in risk assessments and to inform decisions regarding the need for PPE or the decontamination of environmental matrices which may come into contact with agents during research studies. Experiments should be carried out using various pathogen types (e.g., bacteria, viruses, fungi, etc.) and properties (e.g., enveloped & non-enveloped viruses, Gram-positive & -negative bacteria, etc.) for which similar data are not already available and in a variety of matrices relevant to different types of research (e.g., hard surfaces present in standard lab spaces, plants and soil present in greenhouses, matrices associated with field research sites, etc.).

Table 100. Notional Research Design for Stability of Biological Agents in/on Various Matrices	
Research Goal	To generate data on the stability of biological agents on surfaces and in various matrices
Key Variables	• Biological agent type and concentration • Porous (e.g., wood, rubber, cloth) vs. non-porous (e.g., steel, plastic, glass) surfaces • Sample matrix (e.g., soil, water, animal feces, plant litter, etc.) • Sampling method and schedule (e.g., daily, weekly, etc.) • Environmental conditions (e.g., temperature, sunlight, relative humidity, pH, etc.)
Example Protocol	1. Inoculate chosen surface or matrix with a known concentration of the target pathogen and maintain under chosen conditions. 2. Sample initially and on a justifiable schedule to determine the concentration of surviving agent present. 3. Continue sampling until the pathogen is no longer recoverable or the chosen experimental endpoint is reached.
Experimental Outputs	Survival curve for a given biological agent in a chosen matrix

11.2.2 Identification and validation of surrogates for pathogenic organisms

The use of a less or non-hazardous surrogate for a pathogenic microorganism is a strategy that can be used to reduce the risks associated with infectious disease research.[12] This is because surrogate organisms are often safer to work with and may be easier to grow and handle in the laboratory.[200] Surrogates have been identified and validated for use in place of some pathogens (e.g., non-pathogenic *Bacillus* sp. are commonly used as surrogates for *B. anthracis*); however, surrogates have not been identified for many bacterial and viral pathogens. As such, there is a need for validated surrogates that can be used in place of more hazardous microbes in a variety of applications. For example, there is a particular need for identification and validation of surrogate organisms for use in the development and validation of decontamination protocols. The use of surrogates for Risk Group 3 and 4 pathogens in the development and validation of decontamination protocols can be especially advantageous because it allows the work to be carried out under field and real-world conditions. Some spore-forming bacteria have been used as surrogates in the development of general decontamination protocols; however, there is a need for identification and validation of surrogate organisms that can be used in place of other specific high-risk pathogens when developing decontamination protocols.[201]

Table 101. Notional Research Design for Surrogates for Pathogenic Organisms

Research Goal	To generate data on potential surrogates for pathogenic microbes
Key Variables	• Biological agent type (e.g., bacteria, virus, fungus, etc.) • Surrogate attributes (e.g., safety, ease of use, genetics, morphology, growth conditions, etc.) • Surrogate use application (e.g., aerosolization studies, surface survival studies, etc.)
Example Protocol	1. Identify potential surrogates for the pathogen of interest based on practical, biological, and environmental attributes. 2. Validate the surrogate for use in a specific application by comparing its behavior to that of the target pathogen.
Experimental Outputs	Surrogate organism that has been validated for use in a specific application
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Sinclair RG et al. (2012) Criteria for selection of surrogates used to study the fate and control of pathogens in the environment. *Appl Environ Microbiol.* 78 (6)**:** 1969-1977.

Table 102. Notional Research Design for Surrogates for Decontamination Protocols

Research Goal	To generate data on potential surrogates for pathogenic microbes for use in the development of decontamination protocols
Key Variables	• Biological agent type (e.g., bacteria, virus, etc.) and concentration • Surrogate attributes (e.g., safety, ease of use, genetics, morphology, growth conditions, etc.) • Decontamination protocol type (e.g., chemical, non-chemical, etc.)
Example Protocol	2. To validate the use of *Yersinia pseudotuberculosis* as a surrogate for the use of *Y. pestis* in development of decontamination protocols, culture both organisms under identical conditions. 3. Apply disinfectant known to inactivate *Y. pestis* to a known concentration of each species using the appropriate chemical concentration and exposure time (e.g., 10% household bleach for 30 minutes). 4. Apply neutralizing solution.

Table 102. Notional Research Design for Surrogates for Decontamination Protocols	
	5. Plate to recover surviving agent. If no bacteria are recovered, *Y. pseudotuberculosis* may be a good surrogate for development of decontamination protocols for *Y. pestis*. 6. Validate use of *Y. pseudotuberculosis* as a surrogate for development of decontamination protocols for *Y. pestis* by comparing the reaction of both species to disinfectants a sufficient number of times.
Experimental Outputs	Surrogate organism that has been validated for use in lieu of a specific pathogen when developing decontamination protocols.
Reference Studies	The following publications may serve as references for planning and conducting studies related to this data need: • Layman ML, Ramsey CL, Newman SE. (2020) Potential surrogates for evaluation of decontamination methods under field study conditions or BSL-2 biosecurity lab conditions: a review. *Glob J Agric Innov Res Dev.* 7**:** 45-53. • Sinclair RG et al. (2012) Criteria for selection of surrogates used to study the fate and control of pathogens in the environment. *Appl Environ Microbiol.* 78 (6)**:** 1969-1977.

11.2.3 Parameters for personal quarantine periods from animal hosts

A personal quarantine period, sometimes called a personally recognizant quarantine period, is a period of time during which a worker who conducts research with a specific animal pathogen cannot have contact with host species that are susceptible to the agent outside of the containment lab/facility.[202] Regulatory authorities require the implementation of quarantine periods as part of the permitting process for conducting research with certain pathogens of agricultural animals; however, these quarantine periods do not appear to be evidence based.[11,202] The length of a personal quarantine period should be based upon one or more of the following factors: 1) the maximum length of time required for an infected worker to become symptomatic, 2) the maximum length of time that the pathogen of interest can survive on the body or clothing of a worker given exposure conditions (i.e., pathogen amounts), and/or 3) the maximum length of time required for a diagnostic test to return an accurate result, particularly for an asymptomatic individual. This information is readily available for some agents or may be gleaned from an analysis of available case reports for others. In the absence of this information, experimental data are needed to inform the appropriate length of the quarantine period for a given agricultural pathogen.

Table 103. Notional Research Design for Personal Quarantine Periods	
Research Goal	To generate data to inform the need for and/or length of the personal quarantine period for a specific infectious disease
Key Variables	• Target pathogen or disease • Host species • Infection method/route • Availability of diagnostic tests for pathogen identification
Example Protocol	1. Inoculate susceptible hosts with the pathogen at a range of concentrations. 2. Determine the maximum amount of time required for a host to become symptomatic after infection. 3. Validate time value with additional replicates or study rounds.
Experimental Outputs	Validated personal quarantine period for a given pathogen

12. Research Opportunities Related to Risk Mitigation

12.1 Data Needs for Biorisk Mitigation

12.1.1 Metrics for measuring the efficacy of risk mitigations

The assessment, mitigation, and performance (AMP) model of biorisk management involves the assessment of risks associated with the handling of biological agents, the selection and implementation of mitigation measures, and evaluation of the performance of the implemented mitigations to ensure that they are functioning as intended to control risk.[203] Unfortunately, there is currently a lack of data on the effectiveness of risk mitigation measures.[204] Thus, there is a need to define metrics that can be used to demonstrate the performance of mitigation measures that have been implemented to reduce the risk associated with the use of biological agents. Metrics should be defined for the variety of specific mitigation measures (e.g., performing procedures inside a BSC, purchase and use of safety sharps, use of specific PPE items, implementation of training programs, etc.).

Table 104. Notional Research Design for Defining Metrics for Measuring the Efficacy of Mitigations

Research Goal	To generate data on metrics that demonstrate the performance of mitigation measures
Key Variables	• Lab type/level (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) and type of work conducted within (e.g., standard benchwork, animal housing, use of plants, etc.) • Specific mitigation measures implemented • Metric type (e.g., descriptive, threshold, trended, leading, lagging, qualitative, quantitative, etc.) • Value/standard to which each metric is compared • Length of time over which performance is assessed
Example Protocol	1. Develop a list of mitigation measures that are commonly implemented to control biorisks. 2. For each identified mitigation measure, define a set of potential metrics for measuring the performance of the mitigation measure and value/standard to which each metric should be compared. 3. Use each metric to measure the performance of the control measure over the selected period. 4. Once all identified metrics have been tested, compare results to determine which metric(s) successfully measured performance of the implemented control measure over the selected period.
Experimental Outputs	Evidence-based metrics for measuring the performance of specific mitigation measures
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Young S et al. (2014) Measuring Cooperative Biological Engagement Program (CBEP) Performance: Capacities, Capabilities, and Sustainability Enablers for Biorisk Management and Biosurveillance. Prepared for National Defense Research Institute. Santa Monica, CA, USA: RAND Corporation. Available from: https://www.rand.org/pubs/research_reports/RR660.html.

13. Research Opportunities Related to Culture and Communication

13.1 Data Needs for Safety Culture

13.1.1 Factors that influence safety culture in containment laboratories

As mentioned above, development of a strong safety culture within an institution can enhance the efficacy of the entity's biorisk management program; however, there is a lack of information characterizing the factors that can positively influence a culture of safety in microbiological laboratories.[11,12,205,206] Research conducted to develop a culture of safety in non-biorisk management related fields (e.g., construction, healthcare, and oil & gas production) has identified factors that positively impact safety in those disciplines (Kalteh et al, 2019). Studies demonstrate that employee engagement and commitment to safety by leadership are important factors affecting the safety culture in all three of the listed sectors, but that each sector also has specific factors of importance. For example, supervisor priorities are an important factor in oil & gas production, while open communication is important in healthcare settings.[207-209] Similarly, research has shown that factors that influence safety in university laboratories of various types (e.g., biology, chemistry, materials science, engineering, etc.) include the level of risk that workers associate with the laboratory, the principal investigator's attitude toward safety, the design and upkeep of the laboratory space, and the amount and quality of training received by personnel.[210,211] Factors identified as being important to the safety culture in general laboratories can likely be applied to laboratories which use and/or store biological materials; however, additional studies that identify factors specific to containment laboratories are needed to inform further development of a culture of safety within these spaces.[212] Work conducted to provide these data should include different types of institutions, laboratories, and facilities with a range of containment levels, as well as both inexperienced and veteran personnel to ensure that the identified factors are applicable to a wide array of entities that utilize biological agents.

Table 105. Notional Research Design for Factors that May Uniquely Influence Safety Culture in Containment Facilities

Research Goal	To generate data on factors that influence safety cultures in containment laboratories/facilities
Key Variables	• Institution type (e.g., clinical, agricultural, academic, etc.) • Biorisk management program characteristics (e.g., organizational structure, scope, size, etc.) • Containment levels (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) present • Education/Experience of personnel
Example Protocol	1. Perform a review of the safety culture literature to identify factors already shown to influence safety culture in other disciplines. 2. Generate ideas for additional factors that may play a unique role in safety culture at containment facilities, such as the burdens of moving in and out of containment, the motivation to avoid high-consequence pathogen exposures and outbreaks, the leadership style of different levels of management within the institution, or cultural factors related to government or military institutions. 3. Identify a cohort of 10-30 personnel from different types of institutions that use and/or store biohazardous materials to participate in private, anonymized interviews about safety culture. To the extent possible, ensure that personnel work in a variety of different containment levels and have a range of education/experience. 4. Develop an interview protocol that defines safety culture, establishes the factors that have already been recognized as important, and invites participants to reflect and build on those factors in the unique circumstances of containment facilities. Invite participants to consider safety culture factors through the perspective of their particular role in their institution and to consider broad established categories of factors from safety culture research, such as technological supports, social norms, and leadership behavior. If necessary and as the interview

Table 105. Notional Research Design for Factors that May Uniquely Influence Safety Culture in Containment Facilities	
	progresses, the protocol can prompt participants to consider ideas for additional factors that might play a role. 5. Conduct and record interviews, ensuring privacy and anonymity. 6. Transcribe and analyze interviews for themes to identify additional factors that may uniquely influence safety culture in containment facilities. 7. Identify a second cohort of personnel from different types of institutions as in step 3 above. Survey cohort on the factors identified by the interview cohort to validate their wider applicability. 8. Identify a cohort of containment laboratories/facilities of different types. Implement factors identified by personnel in the first phase and determine which factors influence safety culture positively in each setting.
Experimental Outputs	Factors that may uniquely influence safety cultures in containment laboratories/facilities
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Ahadzi DF, Afitiri AR, Ahadzi E. (2021) Organizational safety culture perceptions of healthcare workers in Ghana: A cross-sectional interview study. *Int J Nurs Stud Adv.* 3**:** 100020. • Churruca K et al. (2021) Dimensions of safety culture: a systematic review of quantitative, qualitative and mixed methods for assessing safety culture in hospitals. *BMJ Open.* 11 (7)**:** e043982.

13.1.2 Metrics for evaluating biorisk management safety culture

The current edition of the *LBM* defines safety culture in relation to biorisk management as "values, beliefs, and patterns of behavior instilled and facilitated in an open and trusting atmosphere by individuals and organizations working together to support or enhance best practice for laboratory biosafety".[12] A strong safety culture within an institution is important because it allows for a proactive approach to safety and ultimately impacts the efficacy of the entity's biorisk management program.[11,12] However, while there has been a plethora of attempts to describe the attributes of a strong safety culture, metrics that can be used to assess safety culture are still lacking.[205,206] Thus, there is a need for studies that define and validate metrics of an institution's safety culture as it relates to biorisk management by demonstrating relationships with downstream indicators of risk such as laboratory accidents and improper laboratory practices.

Table 106. Notional Research Design for Metrics for Evaluating Biorisk Management Safety Culture	
Research Goal	To generate data on metrics for evaluating the completeness and/or sophistication of an institution's safety culture as related to biorisk management
Key Variables	• Institution type (e.g., clinical, academic, agricultural, etc.) • Containment levels (e.g., BSL1-4, ABSL1-4, ACL1-4, etc.) present • Proxy variables for risk of biological harms (e.g. lab accident reports or lab inspection records) • Candidate safety-culture metrics (e.g. survey measures of agreement that safety is valued)
Example Protocol	1. Identify proxy variables for risk of harms from laboratory biological agents that can feasibly be collected, such as adherence to biorisk management guidelines as measured by lab inspection records or video data of lab practices. If a variable is based on counts of events, such as lab mistakes or accidents, the baseline rate of these events must be frequent enough for meaningful correlations to be tested with the variable. 2. Identify or develop candidate safety-culture metrics based on literature review or discussions with lab staff. Metrics may include survey measures of beliefs and attitudes (e.g. agreement

Table 106. Notional Research Design for Metrics for Evaluating Biorisk Management Safety Culture	
	that safety is valued, agreement that accidents can be reported without punishment) and/or observational metrics (e.g. presence of appropriate signage in laboratory spaces). 3. Refine measurement strategy for risk proxy variables and candidate safety-culture metrics. For example, develop clear protocols for observational metrics and revise survey question wording and incentives to promote honest responses. 4. Pilot-test risk proxy variables and candidate safety-culture metrics in a small number of labs to validate their utility (e.g. ensure no ceiling or floor effects in data and no logistical issues with data collection). 5. Based on pilot-test results, conduct statistical power analysis to select a target sample size needed to detect a correlation of a target magnitude. 6. Conduct larger-scale data collection to assess correlations between candidate safety-culture metrics and risk proxy variables.
Experimental Outputs	Evidence-based metrics for evaluating the completeness and/or sophistication of an institution's safety culture as related to biorisk management
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Churruca K et al. (2021) Dimensions of safety culture: a systematic review of quantitative, qualitative and mixed methods for assessing safety culture in hospitals. *BMJ Open*. 11 (7): e043982. • Hale AR et al. (2010) Evaluating safety management and culture interventions to improve safety: Effective intervention strategies. *Saf Sci*. 48 (8): 1026-1035. • Perkins D et al. (2019) The culture of biosafety, biosecurity, and responsible conduct in the life sciences: a comprehensive literature review. *Appl Biosaf*. 24 (1): 34-45.

13.1.3 Defining occupational stressors for laboratory personnel

Studies have demonstrated that personnel working in clinical laboratories often experience high levels of stress that can lead to errors, reduced efficiency, poor decision making, and eventual burnout.[213-216] It is likely that individuals working in non-clinical laboratories are similarly impacted by stress and that mitigations are needed to reduce worker stress, thereby reducing errors and increasing safety in the laboratory. As a first step toward developing and implementing mitigations to reduce stress, studies should be conducted to define the various stressors that impact personnel working in research laboratories. Studies carried out to provide these data should consider the stressors associated with different types of research activities (e.g., work with aerosolized agents, work with animals, handling materials with high biological risk, etc.), research performed at different biosafety levels, and the training and experience of the workers.

Table 107. Notional Research Design for Occupational Stressors for Laboratory Personnel	
Research Goal	To define occupational stressors that have negative impacts on personnel working in research laboratories
Key Variables	• Laboratory containment level (e.g., BSL1-4, ABSL1-4, BSL1-4P, ABSL2-4Ag, ACL1-4 etc.) • Research type and procedures performed • Availability of stress relief mechanisms (e.g., opt out periods, rest periods, etc.) • Training/Experience of personnel
Example Protocol	1. Perform a review of the literature to identify stressors that are shown to negatively impact personnel working in other disciplines and in clinical laboratories. 2. Generate ideas for additional stressors that may be uniquely impactful for individuals working in laboratories, such as performing procedures in high- and/or maximum-containment spaces,

Table 107. Notional Research Design for Occupational Stressors for Laboratory Personnel	
	working with animals, performing high risk procedures (e.g., inhalational studies, animal injections, etc.). 3. Identify a cohort of 10-30 personnel with different levels of training/experience that perform different types of research activities at a variety of containment levels to participate in private, anonymized interviews about occupational stressors and their impacts. 4. Develop an interview protocol that defines an occupational stressor, establishes the stressors that have already been recognized as important, and invites participants to reflect and build on those items in the unique circumstances of performing work in containment facilities. If necessary and as the interview progresses, the protocol can prompt participants to consider ideas for additional stressors that might be important. 5. Conduct and record interviews, ensuring privacy and anonymity. 6. Transcribe and analyze interviews for themes to identify stressors that uniquely impact laboratorians.
Experimental Outputs	Occupational stressors that impact personnel working in containment laboratories
Reference Studies	The following publication may serve as a reference when conducting studies related to this data need: • Zhu K, Chen Z. (2024) A qualitative exploration on psychological stressors and coping mechanisms in medical laboratory personnel. *PIJ*. 7 (5): 44-50.

13.2 Data Needs for Communication of Safety Information

13.2.1 Effective communication of safety information

The current edition of the *BMBL* advises posting safety information at the entrance to laboratories and other relevant locations. It also recommends that institutions inform individuals entering containment areas about potential hazards and provide guidance on practices to prevent exposure to biological agents.[11] Unfortunately, conveying this information is complicated by the large number of individuals and diverse roles associated with these spaces (i.e., the scientists, technicians, students, operations and maintenance specialists, and support personnel involved in the biorisk management program as well as the shipping & receiving personnel, equipment technicians, security personnel, occupational health professionals, external inspectors, and other various individuals who may enter containment spaces on an infrequent basis). Different individuals possess varying levels of background knowledge and distinct information needs. Thus, studies are needed to determine the most effective method(s) of communicating safety information tailored to individuals in each role.

Table 108. Notional Research Design for Effective Communication of Safety Information	
Research Goal	To generate data on effective methods for communicating biorisk management safety information to individuals in various roles

Key Variables	• Type of safety information being communicated (e.g., awareness raising, general hazard information, step-by-step procedures, etc.)
	• Role and education/experience of individual receiving safety information
	• Method of communicating safety information:
	  ○ Verbal (e.g., conversation, in-person training session, etc.)
	  ○ Written (e.g., signage, standard operating procedure, etc.)
	  ○ Visual (e.g., infographic, symbology, video, etc.)
	• Method for assessing efficacy of communication methods (e.g., survey, test, Q & A, etc.)

Table 108. Notional Research Design for Effective Communication of Safety Information	
Example Protocol	1. Conduct initial interviews with laboratory staff to understand issues with existing safety information (e.g. it is unclear, not well-targeted, easily ignored, or too time-consuming). 2. Identify the safety information (e.g., hazard information, PPE donning & doffing, emergency evacuation route, etc.) that must be communicated to individuals of each type of role. 3. Develop methods of assessing individuals' knowledge of all safety information, such as scorable written knowledge tests or behavioral assessments. Pilot-test all methods to ensure clarity and avoid ceiling effects (e.g., if participants can infer the correct answer directly from the test without needing to be provided with additional safety information). 4. Devise alternative methods of communicating relevant information based on the interview results and measurement methods described above (e.g., simplified signs that get changed on a schedule). 5. Conduct power analysis to estimate appropriate sample size for detecting plausible or desired effects on outcome measures. 6. Recruit labs with individuals of relevant roles, randomly assigning labs to either a control condition or modified communications. 7. Assess knowledge of relevant information in treatment and control labs before implementing changes and after an appropriate timespan to judge the sustained efficacy of communication methods. Conduct follow-up interviews to assess unintended consequences (e.g. added logistical burdens) as needed.
Experimental Outputs	Effective methods for communicating safety information to individuals in different roles

14. Research Opportunities Related to Personnel and Training

14.1 Data Needs for Human Factors

14.1.1 Understanding the effect of physical stressors on performance of personnel working in high-containment laboratories

Personnel working in high- and maximum-containment laboratories (e.g., BSL3 and BSL4) experience numerous stressors that may affect the accuracy and safety of their work. For example, workers are required to wear PPE which can cause physical stress (e.g., increased body temperature, restricted movement, and difficulty breathing through a respirator), and personnel do not have access to food and water during their shifts.[217,218] Over time, these physical stressors could cause laboratory workers to make mistakes during laboratory procedures leading to potential exposures through spills or needlesticks. There are currently no recommendations for the length of time that laboratory personnel can work in containment conditions. Thus, studies are needed to determine the amount of time laboratorians can work under these conditions before they begin to make mistakes that could impact the safety and security of the laboratory and its personnel.

Table 109. Notional Research Design for Effect of Physical Stressors on Performance of Laboratory Workers in Containment Laboratories	
Research Goal	To generate data on the effects of physical stressors on workers in containment laboratories to inform the development of limits for maximum time in containment
Key Variables	• Training, experience, and physical condition of laboratory personnel • Laboratory/facility type (e.g., standard laboratory, animal facility, etc.) and level (i.e., CL, PC, BSL, ABSL, etc.)

Table 109. Notional Research Design for Effect of Physical Stressors on Performance of Laboratory Workers in Containment Laboratories	
	• Procedures (e.g., bench work, large animal handling, etc.), equipment, and instruments used in the laboratory • PPE ensemble (e.g., coveralls vs. positive pressure suit, powered air purifying respirator vs. N95 respirator, etc.) • Amount of time in containment (e.g., one hour up to a full working shift) • Environmental conditions (i.e., ambient temperature and relative humidity) in the laboratory • Method for measuring incidents (e.g., fluorescent tracer and UV light, continuous video monitoring, etc.)
Example Protocol	1. Set up a mock laboratory with the fixtures, equipment, and instruments typically present in a high-containment laboratory with the addition of video cameras intended to record all activities carried out in the laboratory. 2. Identify appropriately trained personnel with relevant experience who are in good physical condition. 3. Have personnel don the selected PPE ensemble and enter the laboratory. 4. Have personnel perform common laboratory procedures for the selected amount of time (e.g., up to a full working shift) while being continuously monitored for mistakes via video. 5. Have personnel provide information about the physical impacts of the environment on their bodies and have participants call out when they believe a mistake is made. 6. Repeat this process for additional laboratorians until enough data is collected to determine the approximate time at which mistakes begin to occur.
Experimental Outputs	Effects of physical stressors on workers in containment laboratories; approximate amount of time personnel can work in containment before conditions result in increased mistakes
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Perry CM et al. (2008) Effects of physical workload on cognitive task performance and situation awareness. *Theor Issues Ergonomics Sci.* 9 (2)**:** 95-113.

14.2 Data Needs Related to Human Reliability

14.2.1 Rates of human errors in lab procedures

Human error is responsible for the majority of incidents that occur in high-containment laboratories and is a leading cause of pathogen exposures for lab workers.[219] Comprehensive studies of human errors in the laboratory have not yet been conducted; however, Gryphon Scientific used similar studies from other industries to develop a classification system for the types of human errors that may occur in a laboratory setting. These error categories include rule-based human errors that occur when the individual does not adhere to known procedures, skill-based human errors that occur due to issues with motor skills, and knowledge-based errors that can be attributed to a lack of knowledge or experience.[219,220] Extensive research into the types and frequencies of rule-, skill-, and knowledge-based errors that occur during work with pathogens is needed to assess the true risks associated with the study of biological agents and to inform the refinement of laboratory practices and training programs. Studies should assess human errors related to the performance of laboratory methods, as well as adherence to SOPs and relevant policies.

Table 110. Notional Research Design for Rates of Rule-Based Human Errors in Autoclaving Procedures	
Research Goal	To generate data on the rates of rule-based human errors during autoclave procedures
Key Variables	• Lab-specific autoclave SOPs • Factors related to lab personnel being assessed (e.g., training, experience, etc.) • Method for measuring for errors
Example Protocol	1. Train personnel on autoclave SOP. 2. Have lab personnel carry out procedure independently. 3. Measure for adherence to SOP during autoclave activity.
Experimental Outputs	Types and frequencies of rule-based human errors related to autoclave procedures

Table 111. Notional Research Design for Rates of Skill-Based Human Errors in Lab Procedures Involving Pipetting	
Research Goal	To generate data on the rates of skill-based human errors in lab procedures involving pipetting
Key Variables	• Lab procedure being assessed • Factors related to lab personnel being assessed (e.g., training, experience, etc.) • Method for measuring for errors
Example Protocol	1. Add fluorescent dye to samples without lab personnel's knowledge. 2. Have lab personnel pipette samples in accordance with lab procedures. 3. After completion of procedures, look for fluorescent contamination in the lab space.
Experimental Outputs	Types and frequencies of skill-based human errors related to a specific lab procedure

Table 112. Notional Research Design for Rates of Skill-Based Human Errors in Lab Procedures	
Research Goal	To generate data on the rates of knowledge-based human errors during centrifuge procedures
Key Variables	• Lab procedure being assessed • Equipment specific to centrifuge use (e.g., regular caps, aerosol-tight caps, regular rotor lids, gasketed rotor lids, etc.) • Factors related to lab personnel being assessed (e.g., training, experience, etc.) • Method for measuring for errors
Example Protocol	1. Have lab personnel select appropriate equipment and carry out a given centrifuge procedure. 2. Measure the number of errors committed by personnel. 3. Determine if individuals with more experience commit fewer errors than those with less experience.
Experimental Outputs	Types and frequencies of knowledge-based human errors related to centrifuge procedures

14.3 Data Needs for Worker Health Programs

14.3.1 Frequency of Medical Surveillance

Per the U.S. Occupational Safety and Health Administration (OSHA), medical surveillance is the process of analyzing an individual's health data to identify and target issues within the workplace.[221] Current editions of the *BMBL* and *LBM* recommend that laboratory personnel working at BSL-2 and above be provided with risk-based medical surveillance to identify potential laboratory acquired

infections (LAIs); however, there is no evidence-based recommendation for the frequency with which medical surveillance should be conducted.[11,12] Determination of evidence-based frequency for medical surveillance will first require an understanding of the true frequency of LAIs among laboratory workers. To establish this frequency, workers from different labs that perform work with different pathogens in different geographic areas should receive frequent surveillance testing, on a volunteer basis, so that a baseline LAI frequency can be determined.

Table 113. Notional Research Design for Determination of Frequency of Medical Surveillance for Laboratory Workers

Research Goal	To understand the frequency of LAIs among laboratory workers to inform the determination of an evidence-based frequency for medical surveillance
Key Variables	• Biological agent(s) worked with • Frequency of work with agent and procedures used (e.g., generation of aerosols, use of sharps, etc.) • Infection route • Symptoms of infection • Known exposures or losses of containment • Frequency of surveillance testing (e.g., weekly, monthly, etc.), diagnostic test type, and length of project (e.g., one year, two years, etc.) • Availability of diagnostic test for each biological agent
Example Protocol	1. Recruit a broad range of volunteers who work with different biological agents, in different laboratories, in different geographic areas. 2. Test volunteers for infection by the agent(s) they work with on the chosen schedule for the length of the project. 3. Have volunteers report any known exposures or losses of containment. 4. If a test is positive, attempt to determine when and how the infection occurred. 5. Use data to develop an evidence-based frequency that will allow medical surveillance to identify the majority of LAIs.
Experimental Outputs	Frequency of LAIs among laboratory workers; evidence-based frequency for medical surveillance
Reference Studies	The following publication may serve as a reference for planning and conducting studies related to this data need: • Blacksell SD et al. (2024) Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review. *Lancet Microbe.* 5 (2)**:** e194-e202.

14.3.2 Parameters for Post-Exposure Quarantine Periods

A post-exposure quarantine period is a duration of time during which an individual with known exposure to a biological agent isolates to prevent the spread of disease to other susceptible hosts.[222] Worker health programs often include a requirement for an individual to quarantine or self-isolate after a known exposure to a biological agent that causes serious disease in humans and can be readily transmitted between individuals. The length of a post-exposure quarantine period should be based upon one or more of the following factors: 1) the maximum length of time required for an infected worker to become symptomatic, 2) the maximum length of time that the pathogen of interest can survive on the body or clothing of a worker given exposure conditions (i.e., pathogen amounts), and/or 3) the maximum length of time required for a diagnostic test to return an accurate result, particularly for an asymptomatic individual. This information is readily available for some agents or may be gleaned from an analysis of available case reports for others. In the absence of this

information, experimental data are needed to inform the appropriate length of the quarantine period for a given pathogen.

Table 114. Notional Research Design for Post-Exposure Quarantine Periods	
Research Goal	To generate data to inform the need for and/or length of a post-exposure quarantine period for a specific biological agent
Key Variables	• Target biological agent • Infection method/route • Availability of diagnostic test for pathogen identification
Example Protocol	1. Inoculate susceptible animal hosts with the pathogen at a range of concentrations. 2. Determine the maximum amount for a host to become symptomatic after infection. 3. Validate time value with additional replicates or study rounds.
Experimental Outputs	Validated post-exposure quarantine period for a given pathogen

14.4 Data Needs for Training

14.4.1 Appropriate biorisk management topics for institutional and laboratory-specific training sessions

Personnel working in biological laboratories receive training in a variety of topics including general principles of biorisk management (e.g., risk assessment, risk mitigation, performance evaluation, etc.), common biorisk management practices (e.g., handwashing, PPE donning & doffing, purpose of engineering controls, decontamination, etc.), biocontainment, security, incident response, and role-specific training covering the responsibilities assigned to each individual.[66] Biorisk management professionals and laboratory directors/managers often provide these trainings through a combination of institutional training sessions (e.g., a large group of personnel receiving the same training at the same time) and smaller laboratory-specific trainings (e.g., small group training of personnel who work within a single laboratory or facility). However, it is unclear whether the training methodology (i.e., institutional vs. laboratory-specific) impacts the efficacy of training for each topic. As such, studies are needed to determine which training topics are amenable to large group sessions and those that require delivery in a small group setting to be effective.

Table 115. Notional Research Design for Appropriate Biorisk Management Topics for Institutional and Laboratory-Specific Training Sessions	
Research Goal	To determine the biorisk management training topics that can be delivered effectively via large group and small group training sessions
Key Variables	• Training topic (e.g., biohazard spill clean-up, infectious waste collection and treatment, centrifuge use, etc.) • Trainee group size • Method for assessing training efficacy (e.g., pre-/post-assessment, delayed evaluation, observation, etc.)
Example Protocol	1. Identify a relevant pool of training topics commonly provided to laboratory personnel and perform literature reviews and/or survey biorisk management professions to determine how training on each topic is typically delivered. 2. For each topic, design trainings to be delivered at the institutional and laboratory-specific levels.

Table 115. Notional Research Design for Appropriate Biorisk Management Topics for Institutional and Laboratory-Specific Training Sessions	
	3. Identify a cohort of biorisk management programs to provide training on the selected topics at the institutional level and another cohort to provide training at the laboratory-specific level. 4. Assess the efficacy of each training using the selected method. 5. Use data to determine which training topics can be delivered effectively in large group sessions and those that require delivery in a small group.
Experimental Outputs	Evidence-based best practices for delivery of biorisk management-related trainings to large and small groups of trainees

14.4.2 Length of probationary periods for new lab personnel

Laboratory incidents are associated with a variety of factors, including inadequate proficiency of laboratory workers due to lack of education and/or experience, lack of comprehension of training, or failure to adhere to standard operating procedures.[12] Therefore, it is imperative that laboratory personnel receive training specific to their job duties and demonstrate proficiency for procedures that they will perform before working without direct supervision.[11,12,223] The time needed for a new laboratory worker to reach proficiency for assigned procedures is often referred to as a mentorship, proficiency, or training period. Many institutions require new personnel to undergo a period of supervised training before they are permitted to work freely; however, there are no guidelines that indicate how long it typically takes for an individual to gain competency in laboratory procedures and, consequently, how long probationary periods for new laboratory personnel should be. Thus, studies are needed to determine how long probationary periods should be for laboratories of different types and containment levels. Additionally, research conducted to provide these data should consider the education and/or experience of the staff members being assessed, the complexity of the procedures the staff members are expected to perform (e.g., simple procedures such as streaking agar plates vs. more complex procedures like performing animal infections), and the required level of proficiency in the context of the laboratory containment level and the biological agents in use (e.g., intermediate proficiency may be acceptable for personnel working in a standard BSL2 laboratory while an advanced or expert level of proficiency may be necessary for working in a high- or maximum-containment laboratory).[224] Evidence-based probationary periods should not replace individualized assessments of proficiency; rather, a broader and data-driven understanding of the time required to achieve proficiency can support institutions that use probationary periods in shaping effective training and evaluation practices.

Table 116. Notional Research Design for Length of Probationary Periods for New Laboratory Personnel	
Research Goal	To generate data on the length of supervised training time needed for new laboratory personnel to reach proficiency
Key Variables	• Laboratory containment level and risks associated with biological agents in use • Complexity of laboratory procedures in use • Education/experience of new personnel, including previous time spent working in similar or different laboratories • Training method (e.g., in-person demonstration, webinar-based, demonstration, etc.) • Required level of proficiency (e.g., intermediate, advanced, expert, etc.) (NIH Office of Human Resources, 2024) • Method for measuring proficiency (e.g., tests, observation, performance evaluations, etc.)[225]

Table 116. Notional Research Design for Length of Probationary Periods for New Laboratory Personnel	
Example Protocol	1. Identify procedures routinely conducted in laboratories of different containment levels and design methods for training of new personnel to carry out each procedure. Identify experts in each procedure to provide new personnel with training. 2. Identify a cohort of new laboratory personnel with various levels of education/experience (e.g., individuals with no education/ experience in laboratory work, individuals with some education/experience in laboratory work, and individuals with significant education/experience in laboratory work). Divide individuals into the number of groups needed. 3. Have new laboratory personnel receive training on each designated procedure in accordance with the methods developed. 4. When an individual has completed training on a procedure, measure his/her proficiency using the selected method. a) If the individual meets the desired level of proficiency, document the time required to become proficient at that procedure. b) If the individual does not meet the desired level of proficiency, repeat the process until the desired level of proficiency is met. 5. Once all personnel have completed training and demonstrated the desired level of proficiency, use the data to determine the average time required for an individual with given education/experience to work proficiently at a given containment level.
Experimental Outputs	Length of supervised training time needed for new laboratory personnel to reach proficiency; evidence-based recommendation for the length of probationary periods for new laboratory personnel
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Gerbasi S. (2000) Competency assessment in a team-based laboratory. *MLO Med Lab Obs*. 32 (9). • Sharp SE, Elder BL. (2004) Competency Assessment in the Clinical Microbiology Laboratory. *Clin Microbiol Rev.* 17 (3)**:** 681-694.

14.4.3 Frequency of retraining for laboratory personnel

The current edition of the *BMBL* recommends that laboratory personnel receive training initially and that this training be updated whenever the information or procedures change or on an annual basis thereafter.[11] Similarly, U.S. regulations related to laboratory activities involving BBPs and select agents and toxins require this annual refresher training.[226-230] However, these documents do not provide evidence or data that supports this one-year timeline for re-training of personnel is based upon. It is possible that personnel retain training content for longer than the suggested one-year period. Conversely, there is a lack of experimental data to indicate that retraining is not needed on a more frequent basis. Thus, there is a need for real world data regarding how long personnel retain the content of training to inform an evidence-based recommendation for the frequency with which personnel should be retrained on biorisk management-related topics. Research conducted to provide these data should consider the education and/or experience of the staff members being trained, the complexity of the topics and/or procedures covered in the training, and the training method(s) used.

Table 117. Notional Research Design for Frequency of Retraining	
Research Goal	To generate data on the length of time that personnel retain the content of training to inform an evidence-based recommendation for the frequency of retraining
Key Variables	• Education/Experience of personnel receiving training • Training topic and complexity (e.g., general awareness, step-by-step procedure, etc.) • Training method (e.g., virtual or live classroom lecture, webinar or video-based, hands-on interactive, drill, tabletop exercise, etc.) • Method for assessing training efficacy (e.g., pre-/post-assessment, delayed evaluation, observation, etc.) • Assessment schedule (e.g., monthly, every three months, etc.) and project length (e.g., one year, three years, etc.)
Example Protocol	1. Select 5-10 training topics that are typically covered in biorisk management programs and select training methods to be used. For each topic, design separate trainings using the selected methods. 2. Identify a large cohort of laboratory personnel with different levels of education and experience. Divide individuals into the number of groups needed and assign each group to training topic and method combination. 3. Conduct all trainings and use the selected method to assess the efficacy of the training immediately after completion. 4. On the selected schedule, re-assess personnel to determine to what level the content of the training has been retained. Continue re-assessing personnel on the selected schedule until the assessment indicates a need for retraining or until the selected end date of the project. 5. Use data to determine how long training over each topic is retained, if the training method impacts this retention, and if there are commonalities in the type of information that is not retained (e.g., training is not applicable to the individual's role, the procedure is used infrequently, high complexity procedures, etc.). 6. If information associated with a specific training method is retained longer, perform additional studies to test retention of information for other topics via this method.
Experimental Outputs	Evidence-based frequency for re-training of laboratory personnel

14.4.4 Developing metrics of training effectiveness

Educators are often recommended to design their curricula "backwards" by developing assessments of student knowledge and then designing learning experiences intended to improve assessment scores[231]. When educators derive their curricula from high-quality assessments, they tend to stay focused on the most important content, and they can evaluate and improve their work more easily. Unfortunately, there are few high-quality assessments of biorisk management knowledge and practice. High-quality assessments are reliable (scores are stable across reviewers and across repeated assessments in the absence of training), valid (scores precisely measure what they are intended to measure with minimal bias or potential for cheating), and generalizable (scores correlate as expected with other related variables).[232] Self-reports of knowledge and understanding tend to be unreliable, and in-person hands-on assessments can be expensive and difficult to scale.[233,234] There is a need to develop scalable, repeatable assessments of all aspects of biorisk management knowledge and practice that can be used as a framework to evaluate and compare training programs.

Table 118. Notional Research Design for Developing Metrics of Training Effectiveness	
Research Goal	To generate reliable, valid, generalizable, and practically useful assessments that can serve as metrics of biorisk management training effectiveness
Key Variables	• Precise descriptions of knowledge and skills to be assessed • Learner roles (staff, researcher, administrator, etc.)
Example Protocol	1. Select topics for assessment development. 2. Thoroughly review existing training and guidance to precisely articulate all key knowledge to be assessed within each topic. 3. Draft candidate assessment questions that map to key elements of knowledge. 4. Pilot-test candidate assessment questions with an appropriate sample of participants with relevant roles. 5. Develop an evaluation scale and use to refine questions to maximize reliability (e.g., by improving the clarity of scoring rubrics), validity (e.g., by reducing potential for cheating), and generalizability (e.g., by adequately covering relevant subtopics). 6. Evaluate the validity of the refined assessment questions by evaluating expected correlations with professional experience and peer judgments of ability.
Experimental Outputs	Validated metrics of biorisk management knowledge and ability for use in evaluating the efficacy of various training methods and delivery models
Reference Studies	The following publications may serve as a reference for planning and conducting studies related to this data need: • Brizee S et al. (2019) Development of a biosecurity checklist for laboratory assessment and monitoring. *Appl Biosaf*. 24 (2): 83-89. • Lane S, Raymond MR, Haladyna TM (eds). (2016) Handbook of Test Development. Second edn. New York, NY, USA: Routledge, Taylor & Francis Group. • Mislevy RJ, Riconscente MM. (2006) Evidence-Centered Assessment Design. In Handbook of Test Development. Downing SM, Haladyna TM (eds.). 61-90. New York, NY, USA: Routledge.

References

1. Gao W et al. (2024) From Biosafety to National Security: The Evolution and Challenges of Biosafety Laboratories. *Laboratories*. Vol. 1, 158-173.

2. Salerno RM, Gaudioso J. (2015) Chapter 1 - Introduction: The Case for Biorisk Management. In *Laboratory Biorisk Management: Biosafety and Biosecurity*. Salerno RM, Gaudioso J (eds.). 1-30. Boca Raton, FL, USA: CRC Press.

3. Phillips GB. (1961) *Technical Study 35: Microbiological Safety in U.S. and Foreign Laboratories*. Vol. Fort Detrick, MD: U.S. Army Chemical Corps Biological Laboratories.

4. Reitman M, Wedum AG. (1956) Microbiological Safety. *Public Health Report.* 71 (7)**:** 659-665.

5. World Health Organization. (1983) *Laboratory Biosafety Manual*. Vol., 1 edn. Geneva, Switzerland: World Health Organization.

6. Richardson J, Barkley W. (1984) Biosafety in Microbiological and Biomedical Laboratories, 1st edn *U.S. Department of Health and Human Services Public Health Service, Centers for Disease Control and Prevention, National Institutes of Health, Atlanta, GA.*

7. Blacksell SD et al. (2023) The Biosafety Research Road Map: The Search for Evidence to Support Practices in Human and Veterinary Laboratories. *Applied Biosafety.*

8. Casagrande R. (2019) Federal Funding for Biosafety Research is Critically Needed. *CSIS Briefs*. Washington, DC, USA: Center for Strategic and International Studies (CSIS).

9. Kimman Tjeerd G, Smit E, Klein Michèl R. (2008) Evidence-Based Biosafety: a Review of the Principles and Effectiveness of Microbiological Containment Measures. *Clinical Microbiology Reviews.* 21 (3)**:** 403-425.

10. Koblentz G et al. (2023) Global BioLabs Report 2023. Prepared for Kings College London and Schar School of Policy and Government, George Mason University. https://www.kcl.ac.uk/warstudies/assets/global-biolabs-report-2023.pdf.

11. Meechan P, Potts J. (2020) Biosafety in Microbiological and Biomedical Laboratories, 6th edn. . *US Department of Health and Human Services Public Health Service, Centers for Disease Control and Prevention, National Institutes of Health, Atlanta, GA. .*

12. World Health Organization. (2020) *Laboratory Biosafety Manual and Associated Monographs*. Vol., 4 edn. Geneva, Switzerland: World Health Organization.

13. Chughtai AA, Chen X, Macintyre CR. (2018) Risk of self-contamination during doffing of personal protective equipment. *American Journal of Infection Control.* 46 (12)**:** 1329-1334.

14. Albano PM et al. (2020) Cross-contamination in Molecular Diagnostic Laboratories in Low- and Middle-income Countries : A Challenge to COVID-19 Testing. *PJP.* 5 (2)**:** 7-11.

15. De Lappe N et al. (2009) Role of subtyping in detecting Salmonella cross contamination in the laboratory. *BMC Microbiology.* 9 (1)**:** 155.

16. Cherry CLA et al. (2015) Proof of Concept: Containment Systems that Prevent Freeze-Dryer Contamination When Lyophilizing Escherichia coli (JM 109). *Drying Technology.* 33 (4)**:** 466-470.

17. Holmes KL. (2011) Characterization of aerosols produced by cell sorters and evaluation of containment. *Cytometry A.* 79 (12)**:** 1000-1008.

18. Kenny MT, Sabel FL. (1968) Particle size distribution of Serratia marcescens aerosols created during common laboratory procedures and simulated laboratory accidents. *Applied microbiology.* 16 (8)**:** 1146-1150.

19. Hersom M, Irsik M, Thrift T. IFAS Extension. (2008) Biosecurity and Biological Risk Management for Livestock Enterprises Prepared for University of Florida, Institute of Food and Agricultural Science. https://www.nifa.usda.gov/sites/default/files/resource/Biosecurity-and-biological-risk-management-for-livestock.pdf.

20. Guan J et al. (2017) Vehicle and Equipment Decontamination During Outbreaks of Notifiable Animal Diseases in Cold Weather. *Applied Biosafety.* 22 (3)**:** 114-122.

21. Conway J, Wu AG, Lipner SR. (2020) Guidance on hand jewelry for prevention of COVID-19 transmission in healthcare settings. *Dermatol Ther.* 33 (6)**:** e14178.

22. Edel E et al. (1998) Impact of a 5-minute scrub on the microbial flora found on artificial, polished, or natural fingernails of operating room personnel. *Nurs Res.* 47 (1)**:** 54-59.

23. Hedderwick SA et al. (2000) Pathogenic organisms associated with artificial fingernails worn by healthcare workers. *Infect Control Hosp Epidemiol.* 21 (8)**:** 505-509.

24. Trick WE et al. (2003) Impact of Ring Wearing on Hand Contamination and Comparison of Hand Hygiene Agents in a Hospital. *Clinical Infectious Diseases.* 36 (11)**:** 1383-1390.

25. Ward DJ. (2007) Hand adornment and infection control. *Br J Nurs.* 16 (11)**:** 654-656.

26. U.S. Centers for Disease Control and Prevention. Fundamentals of Donning and Doffing PPE in Clinical Laboratories. https://www.youtube.com/watch?v=YFrRe16qgUE. Accessed July 29, 2024.

27. U.S. Centers for Disease Control and Prevention. How to Safety Remove Personal Protective Equipment (PPE) - Examples 1 & 2. https://www.cdc.gov/healthcare-associated-infections/media/pdfs/ppe-sequence-p.pdf?CDC_AAref_Val=https://www.cdc.gov/hai/pdfs/ppe/PPE-Sequence.pdf. Accessed July 29, 2024.

28. Sahay N et al. (2022) Risk of self-contamination because of improper doffing of personal protective equipment: A randomised cross-over study. *Indian J Anaesth.* 66 (9)**:** 638-643.

29. Tomas ME et al. (2015) Contamination of Health Care Personnel During Removal of Personal Protective Equipment. *JAMA Intern Med.* 175 (12)**:** 1904-1910.

30. Bennett A, Parks S. (2006) Microbial aerosol generation during laboratory accidents and subsequent risk assessment. *Journal of Applied Microbiology.* 100 (4)**:** 658-663.

31. Miller HE et al. (2014) Characterization of Respirable Aerosols Generated during Routine Laboratory Procedures. *Applied Biosafety.* 19 (1)**:** 19-27.

32. Pottage T et al. (2014) Quantification of Microbial Aerosol Generation during Standard Laboratory Procedures. *Applied Biosafety.* 19 (3)**:** 124-131.

33. Pottage T et al. (2022) Microbial Aerosols Generated from Standard Microbiological Laboratory Procedures. *Applied Biosafety.* 27 (2)**:** 92-99.

34. American Animal Hospital Association. AAHA Guidelines: Performing a Necropsy. https://www.aaha.org/aaha-guidelines/infection-control-configuration/protocols/performing-a-necropsy/. Archived: http://web.archive.org/web/20230703212624/https://www.aaha.org/aaha-guidelines/infection-control-configuration/protocols/performing-a-necropsy/. Accessed March 30, 2023.

35. Wenner L et al. (2017) Aerosol Generation During Bone-Sawing Procedures in Veterinary Autopsies. *Vet Pathol.* 54 (3)**:** 425-436.

36. Ashcroft J, Pomeroy NP. (1983) The generation of aerosols by accidents which may occur during plant-scale production of micro-organisms. *Journal of Hygiene.* 91 (1)**:** 81-91.

37. Dimmick RL. (1973) Laboratory Hazards from Accidentally Produced Airborne Microbes. *Dev Ind Microbiol.* 15**:** 44-47.

38. Dimmick RL, Vogl WF, Chatigny MA. (1974) Potential for Accidental Microbial Aerosol Transmission in the Biological Laboratory. In *Biohazards in Biological Research*. New York: Cold Spring Harbor Laboratory.

39. Burnett LC, Lunn G, Coico R. (2009) Biosafety: Guidelines for Working with Pathogenic and Infectious Microorganisms. *Current Protocols in Microbiology.* 13 (1)**:** 1A.1.1-1A.1.14.

40. Vijayan V, Sern BNB, Johnson B. (2019) Modified Efficient and Simple Method for Biological Spill Cleanup. *Appl Biosaf.* 24 (3)**:** 141-146.

41. National Research Council Committee on Hazardous Biological Substances in the L. (1989). Washington, D.C., USA: National Academies Press

42. Adegoke AA et al. (2018) Epidemiological Evidence and Health Risks Associated With Agricultural Reuse of Partially Treated and Untreated Wastewater: A Review. *Front Public Health.* 6**:** 337.

43. Aguilar-Setién A et al. (2022) Biosafety Practices When Working with Bats: A Guide to Field Research Considerations. *Applied Biosafety.* 27 (3)**:** 169-190.

44. Hawley RJ, Eitzen EM, Jr. (2001) Biological weapons--a primer for microbiologists. *Annu Rev Microbiol.* 55**:** 235-253.

45. Laber K, Kennedy BW, Young L. (2007) Field studies and the IACUC: protocol review, oversight, and occupational health and safety considerations. *Lab Animal.* 36 (1)**:** 27-33.

46. Boyce JM. (2023) Current issues in hand hygiene. *American Journal of Infection Control.* 51**:** A35-A43.

47. U.S. Centers for Disease Control and Prevention USDoA. Federal Select Agent Program - Inspection Checklists https://www.selectagents.gov/compliance/preparing.htm. Last Updated October 31, 2023. Accessed October 19, 2024.

48. Pittet D. (2017) Hand hygiene: From research to action. *J Infect Prev.* 18 (3)**:** 100-102.

49. Stadler RN, Tschudin-Sutter S. (2020) What is new with hand hygiene? *Current Opinion in Infectious Diseases.* 33 (4).

50. Glowicz JB et al. (2023) SHEA/IDSA/APIC Practice Recommendation: Strategies to prevent healthcare-associated infections through hand hygiene: 2022 Update. *Infection Control & Hospital Epidemiology.* 44 (3)**:** 355-376.

51. World Health Organization. (2009) WHO Guidelines on Hand Hygiene in Health Care. Prepared for World Health Organization. https://iris.who.int/bitstream/handle/10665/44102/9789241597906_eng.pdf?sequence=1.

52. Conover DM, Gibson KE. (2016) A review of methods for the evaluation of handwashing efficacy. *Food Control.* 63**:** 53-64.

53. International Air Transport Association. (2024) *IATA Dangerous Good Regulations*. Vol. Montreal, Canada: IATA.

54. World Health Organization. (2021) Guidance on Regulations for the Transport of Infectious Substances 2021-2022. Prepared for. https://iris.who.int/bitstream/handle/10665/339825/9789240019720-eng.pdf?sequence=1.

55. United Nations. (2023) *Recommendations on the Transport of Dangerous Goods - Model Regulations*. Vol., 23rd revised edn. New York and Geneva: United Nations Publications.

56. Shiferaw MB, Yismaw G, Getachew H. (2018) Specimen rejections among referred specimens through referral network to the Amhara Public Health Institute for laboratory testing, Bahir Dar, Ethiopia. *BMC Research Notes.* 11 (1)**:** 781.

57. Budowle B et al. (2006) Quality sample collection, handling, and preservation for an effective microbial forensics program. *Appl Environ Microbiol.* 72 (10)**:** 6431-6438.

58. Farkas DH et al. (1996) Specimen collection and storage for diagnostic molecular pathology investigation. *Arch Pathol Lab Med.* 120 (6)**:** 591-596.

59. Gunn-Christie RG. (2023) Collection and Submission of Laboratory Samples from Animals. *MSD Veterinary Manual*. Rahway, New Jersey: Merck & Co., Inc.

60. Griffiths A et al. (2011) An Electronic Inventory System Designed to Aid Compliance with the National Select Agents Registry Program. *Applied Biosafety.* 16 (1)**:** 9-18.

61. World Health Organization. (2014) Safe Management of Wastes for Health-Care Activities Chartier Y et al (eds). Geneva, Switzerland: WHO Press.

62. Genzen JR. (2020) Wiping the Slate Clean-Assessing Clinical Laboratory Contamination Risk. *Clin Chem.* 66 (9)**:** 1128-1130.

63. Westwood JC, Mitchell MA, Legacé S. (1971) Hospital sanitation: the massive bacterial contamination of the wet mop. *Appl Microbiol.* 21 (4)**:** 693-697.

64. Jones RM et al. (2020) A systematic risk-based strategy to select personal protective equipment for infectious diseases. *American Journal of Infection Control.* 48 (1)**:** 46-51.

65. Eissa ME et al. (2012) Neutralizer Evaluation Study of Some Microbial Isolates Against Two Strong Disinfectants with and Without the Presence of Synthetic Detergent.

66. U.S. Centers for Disease Control and Prevention, U.S. Department of Agriculture Animal and Plant Health Inspection Service. (2021) Guidance for Select Agent Regulation Training Requirements. Prepared for Federal Select Agent Program. https://www.selectagents.gov/compliance/guidance/training/docs/Regulation_Training_Requirements.pdf.

67. Rutala WA, Weber DJ, Healthcare Infection Control Practices Advisor Committee (HICPAC). (2019) Guideline for Disinfection and Sterilization in Healthcare Facilities. Prepared for US Centers for Disease Control and Prevention. https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines-H.pdf.

68. Rhee CH et al. (2023) Chemical stability of active ingredients in diluted veterinary disinfectant solutions under simulated storage conditions. *Frontiers in Chemistry.* Volume 11 - 2023.

69. TECOLAB. How to Prove the Shelf Life and Stability of Disinfectants? https://tecolab-global.com/how-to-prove-the-shelf-life-and-stability-of-disinfectants/. Archived: https://web.archive.org/web/20230223152728/https://tecolab-global.com/how-to-prove-the-shelf-life-and-stability-of-disinfectants/. Accessed January 21, 2025.

70. Artasensi A, Mazzotta S, Fumagalli L. (2021) Back to Basics: Choosing the Appropriate Surface Disinfectant. *Antibiotics (Basel).* 10 (6).

71. Campagna MV et al. (2016) Factors in the Selection of Surface Disinfectants for Use in a Laboratory Animal Setting. *Journal of the American Association for Laboratory Animal Science.* 55 (2)**:** 175-188.

72. Dvorak G. (2005) Disinfection 101. Prepared for Iowa State University Center for Food Security and Public Health. https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=11bab41b95553e7fd9e8d023985c0ea1b79e23f3.

73. Abban S, Jakobsen M, Jespersen L. (2013) A practical evaluation of detergent and disinfectant solutions on cargo container surfaces for bacteria inactivation efficacy and effect on material corrosion. *African Journal of Biotechnology.* 12 (23)**:** 3689-3698.

74. LANXESS. (2022) Virkon S - Vehicle Disinfection Materials Compatibility. Prepared for LANXESS Corporation. https://www.qcsupply.com/media/product_attachments/attachment_file/v/i/virkon_s_vehicle_disinfectant_compatibility.pdf.

75. Teska P et al. Characteristics of an Ideal Surface Damage Testing Protocol. https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Archived: https://web.archive.org/web/20240208164254/https://www.infectioncontroltoday.com/view/characteristics-ideal-surface-damage-testing-protocol. Accessed February 7, 2024.

76. Holah JT et al. (1998) Future techniques for disinfectant efficacy testing. *International Biodeterioration & Biodegradation.* 41**:** 273-279.

77. Tarka P, Nitsch-Osuch A. (2021) Evaluating the Virucidal Activity of Disinfectants According to European Union Standards. *Viruses.* 13 (4).

78. U.S. Department of Agriculture, Iowa State University of Science and Technology. (2014) National Animal Health Emergency Management System (NAHEMS) Guidelines: Cleaning and Disinfection. Prepared for FAD PReP/NAHEMS. https://www.aphis.usda.gov/sites/default/files/cleaning_disfection.pdf.

79. Teuscher AC et al. (2024) Effectiveness of chemical inactivation of infectious liquid biological waste: A randomized sample study of research laboratories in Switzerland. *Journal of Biosafety and Biosecurity.* 6 (1)**:** 16-26.

80. Wichmann F et al. (2017) Monitoring of genetically modified Escherichia coli in laboratory wastewater. *Environmental Science and Pollution Research.* 24 (30)**:** 23725-23734.

81. Klaponski N et al. (2011) A Study of the Effectiveness of the Containment Level-4 (CL-4) Chemical Shower in Decontaminating Dover Positive-Pressure Suits. *Applied Biosafety.* 16 (2)**:** 112-117.

82. Parks SR et al. (2013) Showering BSL-4 Suits to Remove Biological Contamination. *Applied Biosafety.* 18**:** 162 - 171.

83. U.S. Centers for Disease Control and Prevention. Sterilizing Practices: Guideline for Disinfection and Sterilization in Healthcare Facilities https://www.cdc.gov/infectioncontrol/guidelines/disinfection/sterilization/sterilizing-practices.html. Archived: https://web.archive.org/web/20240318182801/https://www.cdc.gov/infectioncontrol/guidelines/disinfection/sterilization/sterilizing-practices.html. Last Updated September 18, 2016. Accessed March 27, 2023.

84. Chang JC et al. (1985) UV inactivation of pathogenic and indicator microorganisms. *Appl Environ Microbiol.* 49 (6)**:** 1361-1365.

85. Kowalski W. (2009) *Ultraviolet Germicidal Irradiation Handbook: UVGI for Air and Surface Disinfection*. Vol. Berlin, Germany: Springer.

86. Raeiszadeh M, Adeli B. (2020) A Critical Review on Ultraviolet Disinfection Systems against COVID-19 Outbreak: Applicability, Validation, and Safety Considerations. *ACS Photonics.* 7 (11)**:** 2941-2951.

87. Kesavan J et al. (2014) UV-C Decontamination of Aerosolized and Surface-Bound Single Spores and Bioclusters. *Aerosol Science and Technology.* 48 (4)**:** 450-457.

88. Rezaie A et al. (2020) Ultraviolet A light effectively reduces bacteria and viruses including coronavirus. *PLoS One.* 15 (7)**:** e0236199.

89. Soh TK et al. (2023) A validated protocol to UV-inactivate SARS-CoV-2 and herpesvirus-infected cells. *PLOS ONE.* 18 (5)**:** e0274065.

90. Adlhart C et al. (2018) Surface modifications for antimicrobial effects in the healthcare setting: a critical overview. *J Hosp Infect.* 99 (3)**:** 239-249.

91. Hasan J, Crawford RJ, Ivanova EP. (2013) Antibacterial surfaces: the quest for a new generation of biomaterials. *Trends Biotechnol.* 31 (5)**:** 295-304.

92. Mullen DC et al. (2021) Precision Design of Antimicrobial Surfaces. *Front Med Technol.* 3**:** 640929.

93. Sheridan M et al. (2022) Biomaterials: Antimicrobial surfaces in biomedical engineering and healthcare. *Current Opinion in Biomedical Engineering.* 22**:** 100373.

94. Reinosa JJ et al. (2022) The challenge of antimicrobial glazed ceramic surfaces. *Ceramics International.* 48 (6)**:** 7393-7404.

95. Schettler T. (2016) Antimicrobials in Hospital Furnishings: Do They Help Reduce Healthcare-Associated Infections? Prepared for Health Care Without Harm. https://noharm-uscanada.org/sites/default/files/documents-files/3854/Antimicrobials%20Report%202016_1.pdf.

96. Bansod HS, Deshmukh P. (2023) Biomedical Waste Management and Its Importance: A Systematic Review. *Cureus.* 15 (2)**:** e34589.

97. Janik-Karpinska E et al. (2023) Healthcare Waste-A Serious Problem for Global Health. *Healthcare (Basel).* 11 (2).

98. Tait PW et al. (2020) The health impacts of waste incineration: a systematic review. *Australian and New Zealand Journal of Public Health.* 44 (1)**:** 40-48.

99. Gautam V, Thapar R, Sharma M. (2010) Biomedical waste management: Incineration vs. environmental safety. *Indian Journal of Medical Microbiology.* 28 (3)**:** 191-192.

100. Manzoor J, Sharma M. (2019) Impact of Biomedical Waste on Environment and Human Health. *Environmental Claims Journal.* 31 (4)**:** 311-334.

101. Sabiha-Javied et al. (2009) Heavy metal pollution from phosphate rock used for the production of fertilizer in Pakistan. *Microchemical Journal.* 91 (1)**:** 94-99.

102. Esmizadeh E et al. (2021) Can Medical-Grade Gloves Provide Protection after Repeated Disinfection? *ACS Applied Polymer Materials.* 3 (1)**:** 445-454.

103. Esmizadeh E et al. (2021) Stability of nitrile and vinyl latex gloves under repeated disinfection cycles. *Materials Today Sustainability.* 11-12**:** 100067.

104. Grillet AM et al. (2020) COVID-19 global pandemic planning: Performance and electret charge of N95 respirators after recommended decontamination methods. *Experimental Biology and Medicine.* 246 (6)**:** 740-748.

105. Kharbat A, Mizer A, Zumwalt M. (2020) Decontamination methods of personal protective equipment for repeated utilization in medical/surgical settings. *The Southwest Respiratory and Critical Care Chronicles.* 8 (34).

106. Zorko DJ et al. (2020) Decontamination interventions for the reuse of surgical mask personal protective equipment: a systematic review. *Journal of Hospital Infection.* 106 (2)**:** 283-294.

107. Houghton C, Saurya S, Foster B. (2022) Taking a LEAF out of the green lab book. *The Biochemist.*

108. Farley M, Nicolet BP. (2023) Re-use of laboratory utensils reduces CO2 equivalent footprint and running costs. *PLOS ONE.* 18 (4)**:** e0283697.

109. Anderson RC. (2002) Sustainable Development: Incentive-Based Policies for Environmental Mangagement in Developing Countries. Prepared for Resources for the Future. https://media.rff.org/documents/RFF-IB-02-07.pdf.

110. Flory GA et al. (2017) Aboveground burial for managing catastrophic losses of livestock. *International Journal of One Health.* 3**:** 50-56.

111. Ebling R et al. (2022) Virus viability in spiked swine bone marrow tissue during above-ground burial method and under in vitro conditions. *Transboundary and Emerging Diseases.* 69 (5)**:** 2987-2995.

112. Miller L, Flory G. (2018) Carcass Management for Small- and Medium- Scale Livestock Farms: Practical Considerations. Prepared for Food and Agriculture Organization of the United Nations. https://www.fao.org/3/CA2073EN/ca2073en.pdf.

113. Kalbasi A et al. (2005) Carcass Composting for Management of Farm Mortalities: A Review. *Compost Science & Utilization.* 13 (3)**:** 180-193.

114. Wilkinson KG. (2007) The biosecurity of on-farm mortality composting. *Journal of Applied Microbiology.* 102 (3)**:** 609-618.

115. Payne J, Pugh B. (2017) ANSI-8220: On-Farm Mortality Composing of Livestock Carcasses. Prepared for Oklahoma Cooperative Extension Service. https://pods.okstate.edu/fact-sheets/ANSI-8220pod.pdf.

116. Lab.Space Construction. How Much Does the Design and Construction of a Laboratory Cost? https://lab.space/faq/how-much-does-the-design-and-construction-of-a-laboratory-cost/. Archived: https://web.archive.org/web/20240701135356/https://lab.space/faq/how-much-does-the-design-and-construction-of-a-laboratory-cost/. Accessed July 1, 2024.

117. Romero S, D'Orlando J. (2023) 2023 Life Sciences Fit Out Cost Guide. Prepared for Cushman & Wakefield. https://cushwake.cld.bz/Life-Sciences-US-Fit-Out-Cost-Guide-2023.

118. U.S. National Institutes of Health. (2024) Design Requirements Manual, Rev. 2.0. https://orf.od.nih.gov/TechnicalResources/Documents/DRM/DRM2.003122024.pdf.

119. Richmond Scientific. Optimising Lab Layout for Productivity: 10 Tips for Success. https://www.richmondscientific.com/efficient-lab-layout. Archived: https://web.archive.org/web/20240702202912/https://www.richmondscientific.com/efficient-lab-layout. Accessed July 2, 2024.

120. Skolozdra RB. How Smart Lab Design and Layout Ensure Optimal Procedures, Workflow, Cooperation, and Productivity. https://www.labmanager.com/it-s-all-in-the-planning-how-smart-lab-design-and-layout-ensure-optimal-procedures-workflow-cooperation-and-productivity-15697. Archived: https://web.archive.org/web/20240702201217/https://www.labmanager.com/it-s-all-in-the-planning-how-smart-lab-design-and-layout-ensure-optimal-procedures-workflow-cooperation-and-productivity-15697. Accessed July 2, 2024.

121. Liu Z et al. (2020) Experimental and numerical study of potential infection risks from exposure to bioaerosols in one BSL-3 laboratory. *Building and Environment.* 179**:** 106991.

122. Liu Z et al. (2020) Effect of equipment layout on bioaerosol temporal-spatial distribution and deposition in one BSL-3 laboratory. *Building and Environment.* 181**:** 107149.

123. Somers AE et al. (2000) Quantifying rubber degradation using NMR. *Polymer Degradation and Stability.* 70 (1)**:** 31-37.

124. Racine T, Kobinger GP. (2019) Challenges and perspectives on the use of mobile laboratories during outbreaks and their use for vaccine evaluation. *Hum Vaccin Immunother.* 15 (10)**:** 2264-2268.

125. Wölfel R et al. (2015) Mobile diagnostics in outbreak response, not only for Ebola: a blueprint for a modular and robust field laboratory. *Euro Surveill.* 20 (44).

126. Xing W et al. (2021) A Highly Automated Mobile Laboratory for On-site Molecular Diagnostics in the COVID-19 Pandemic. *Clinical Chemistry.* 67 (4)**:** 672-683.

127. Qasmi SA et al. (2023) Mobile biosafety level (BSL) 2 laboratories deployment: Strengthening the diagnostic facilities in Pakistan with emerging public health challenges and the way forward. *Journal of Biosafety and Biosecurity.* 5 (2)**:** 79-83.

128. Rao V, Bordelon E. (2019) Mobile High-Containment Biological Laboratories Deployment: Opportunities and Challenges in Expeditionary Deployments to Outbreak Response. *Appl Biosaf.* 24 (1)**:** 20-29.

129. Linster M, Ng B, Vijayan V. (2020) COVID-19 and Beyond: Safety and Design Considerations for the Development of a Mobile Biocontainment Laboratory. *Appl Biosaf.* 25 (3)**:** 169-173.

130. Kozlovac J, Schmitt B. (2015) Biosafety principles and practices for the veterinary diagnostic laboratory. *Methods Mol Biol.* 1247**:** 31-41.

131. Freese T et al. (2024) The relevance of sustainable laboratory practices. *RSC Sustain.* 2 (5)**:** 1300-1336.

132. Kitzberger T, Kotik J, Pröll T. (2022) Energy savings potential of occupancy-based HVAC control in laboratory buildings. *Energy and Buildings.* 263**:** 112031.

133. U.S. Environmental Protection Agency, U.S. Department of Energy. (2008) Laboratories for the 21st Century: An Introduction to Low-Energy Design. Prepared for National Renewable Energy Laboratory. https://www.nrel.gov/docs/fy08osti/29413.pdf.

134. Dobbelaere J, Heidelberger JB, Borgermann N. (2022) Achieving sustainable transformation in science - green grassroots groups need nurturing from the top. *J Cell Sci.* 135 (17).

135. My Green Lab. Energy. https://www.mygreenlab.org/energy.html. Archived: https://web.archive.org/web/20250114213216/https://www.mygreenlab.org/energy.html. Accessed January 14, 2024.

136. British Standards Institute. (2000) BS EN 12469:2000 Biotechnology - Performance Criteria for Microbiological Safety Cabinets. London, England: British Standards Institute

137. NSF International, American National Standards Institute. (2022) NSF/ANSI 49-2022 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification. Ann Arbor, Michigan, USA: NSF International.

138. Feng X et al. (2019) Aerosol containment by airflow in biosafety laboratories. *Journal of Biosafety and Biosecurity.* 1 (1)**:** 63-67.

139. Kurth A, Weber U, Reichenbacher D. (2022) Maintaining differential pressure gradients does not increase safety inside modern BSL-4 laboratories. *Front Bioeng Biotechnol.* 10**:** 953675.

140. Aircuity. (2012) Laboratory Ventilation ACH Rates - Standard and Guidelines Prepared for Aircuity, Inc. https://www.aircuity.com/wp-content/uploads/Aircuity-White-Paper_Lab-Ventilation-ACH-Rates_Standards-Guidelines_ACHWP_20120103-2.pdf.

141. Pastorino B, de Lamballerie X, Charrel R. (2017) Biosafety and Biosecurity in European Containment Level 3 Laboratories: Focus on French Recent Progress and Essential Requirements. *Front Public Health.* 5**:** 121.

142. Jennette J, Grimaldo M, Henneman J. (2014) Containment Talk - Direction Airflow - Where (and When) Do We Need It? *Applied Biosafety.* 18 (1)**:** 40-41.

143. American National Standards Institute, American Society of Safety Professionals. (2020) ANSI/ASSP Z9.14 - 2020 Testing and Performance-Verification Methodologies for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Ventilation Systems. Park Ridge, Illinois, USA: ASSP.

144. Government of Canada. (2022) Canadian Biosafety Standard For Facilities Handling or Storing Human and Terrestrial Animal Pathogens and Toxins, Third Edition.

145. Mittal H et al. (2011) Survival of Microorganisms on HEPA Filters. *Applied Biosafety.* 16 (3)**:** 163-166.

146. NuAire. Air Filtration and the Use of HEPA Filters in Biological Safety Cabinets. https://www.nuaire.com/resources/hepa-filters-in-biosafety-cabinets.

147. Youth Cleanroom Solutions. The Comprehensive Gujide to Bag-in-Bag-Out (BIBO) HEPA Filter Replacement https://youthfilter.com/news/the-comprehensive-guide-to-bag-in-bag-out-bibo-hepa-filter-replacement/#products. Archived: https:///web/20240722150034/https://youthfilter.com/news/the-comprehensive-guide-to-bag-in-bag-out-bibo-hepa-filter-replacement/#products. Accessed July 22, 2024.

148. Baron JL. (2023) Ask the Experts: Biosafety Cabinet Gas Decontamiantion Considerations. Prepared for NuAire, Inc. . https://www.nuaire.com/resources/biosafety-cabinet-gas-decontamination-considerations.

149. Thermo Scientific. Technical Note: Biological Safety Cabinets - Fumigation Methodologies https://assets.thermofisher.com/TFS-Assets/LED/Warranties/BSC-Fumigation-Technical-Note.pdf. Archived: https://web.archive.org/web/20231226090956/https://assets.thermofisher.com/TFS-Assets/LED/Warranties/BSC-Fumigation-Technical-Note.pdf. Accessed January 13, 2025.

150. Heckert RA et al. (2011) International Biosafety and Biosecurity Challenges: Suggestions for Developing Sustainable Capacity in Low-resource Countries *Appl Biosaf.* 16 (4)**:** 223-230.

151. Held K, Thibeault R. (2020) Multiple users in a biosafety cabinet compromise containment. Prepared for The Baker Company. https://bakerco.com/wp-content/uploads/2020/03/Multiple-users-in-a-Biosafety-Cabinet-compromise-containment-White-Paper-Download.pdf.

152. Hinrichs T, Gragert S, Klein M. (2016) Biological Safety Cabinets: Simulation and Quantifying of Airflow Perturbation Caused by Personnel Activities. *Applied Biosafety.* 21 (1)**:** 12-18.

153. Parks S et al. (2022) The Impact of Air Inflow and Interfering Factors on the Performance of Microbiological Safety Cabinets. *Appl Biosaf.* 27 (1)**:** 23-32.

154. The Baker Company. (2023) BSC Mythbusters - How Much Space is Required Around a Biosafety Cabinet to Maintain Proper Protection [Video]. . https://www.youtube.com/watch?v=DeWmavEp3wc.

155. Burgener J. (2006) Position Paper on the Use of Ultraviolet Lights in Biological Safety Cabinets. *Applied Biosafety.* 11 (4)**:** 228-230.

156. Held K. (2020) BSC MythBusters: Can I Use UV or Any Chemials as a Disinfectant in my BSC? Prepared for The Baker Company. https://bakerco.com/wp-content/uploads/2020/03/Can-I-use-UV-or-any-chemical-as-a-disinfectant-in-my-BSC.pdf. .

157. Labconco Corporation. User's Manual-Purifier® Logic+ Biological Safety Cabinets. https://physiology.case.edu/media/eq_manuals/eq_manual_labconco_a2_logic_plus_users_manual.pdf.

158. De Penning S. Biosafety Cabinet Types. https://www.nuaire.com/resources/biosafety-cabinet-types-article. Archived: https://web.archive.org/web/20250515153447/https://www.nuaire.com/resources/biosafety-cabinet-types-article. Accessed May 15, 2025.

159. Behrmann T et al. (2007) Regulatory Compliance of a BSL-3 Laboratory Unit in a Drug Discovery Environment. *Applied Biosafety.* 12 (4)**:** 220-238.

160. Cleanroom Technology. Autoclave Design for the Pandemic Era. https://cleanroomtechnology.com/autoclave-design-for-the-pandemic-era-170886. Archived: https://web.archive.org/web/20240816201824/https://cleanroomtechnology.com/autoclave-design-for-the-pandemic-era-170886. Accessed August 16, 2024.

161. The University of Texas Rio Grande Valley. Biosafety Levels 1, 2, 3, & 4. https://www.utrgv.edu/ehsrm/programs/lab-safety/biological-safety-program/biosafety-levels/index.htm. Archived: https://web.archive.org/web/20231203064016/https://www.utrgv.edu/ehsrm/programs/lab-safety/biological-safety-program/biosafety-levels/index.htm. Accessed August 16, 2024.

162. Gassiep I et al. (2021) Laboratory Safety: Handling Burkholderia pseudomallei Isolates without a Biosafety Cabinet. *J Clin Microbiol.* 59 (7)**:** e0042421.

163. U.S. Federal Select Agent Program. Policy Statement: BSL-3/ABSL-3 Verification. https://www.selectagents.gov/regulations/policy/bsl3absl3.htm. Archived: https://web.archive.org/web/20240926204749/https://www.selectagents.gov/regulations/policy/bsl3absl3.htm. Last Updated November 20, 2014. Accessed September 26, 2024.

164. U.S. Federal Select Agent Program. Policy Statement: Biosafety Level 4 (BSL-4)/Animal BSL-4 (ABSL-4) Laboratory FAcility Verification Requirements. https://www.selectagents.gov/regulations/policy/BSL4ABSL4.htm. Archived: https://web.archive.org/web/20240926205135/https://www.selectagents.gov/regulations/policy/BSL4ABSL4.htm. Last Updated February 9, 2023. Accessed September 26, 2024.

165. Osborne R et al. (1999) Performance of open-fronted microbiological safety cabinets: the value of operator protection tests during routine servicing. *Journal of Applied Microbiology.* 86 (6)**:** 962-970.

166. Swearengen JR, Holt RK, Bowman RL. (2018) Chapter 30: Managing Husbandry Programs Involving Experimental Hazards. In *Management of Animal Care and Use Programs in Research, Education, and Testing*. Weichbrod RH, Thompson GAH, Norton JN (eds.). Boca Raton, FL: CRC Press/Taylor & Francis.

167. U.S. National Institutes of Health. (2011) Local Exhaust Ventilation Testing Protocols Prepared for NIH. https://ors.od.nih.gov/sr/dohs/Documents/nih-local-exhaust-ventilation-testing-protocols.pdf.

168. Whistler T, Kaewpan A, Blacksell SD. (2016) A Biological Safety Cabinet Certification Program: Experiences in Southeast Asia. *Appl Biosaf.* 21 (3)**:** 121-127.

169. U.S. Centers for Disease Control and Prevention. Best Practices for Sterilization Monitoring in Dental Settings. https://www.cdc.gov/dental-infection-control/hcp/dental-ipc-faqs/sterilization-monitoring.html#:~:text=A%20spore%20test%20should%20be,Sterilization%20records. Archived: https://web.archive.org/web/20250707234947/https://www.cdc.gov/dental-infection-control/hcp/dental-ipc-faqs/sterilization-monitoring.html. Accessed July 7, 2025.

170. George Mason University Environmental Health & Safety. (2015) Autoclave Safety Guide. https://ehs.gmu.edu/wp-content/uploads/2015/03/AutoclaveSafetyGuide.pdf.

171. University of Washington Environmental Health & Safety. (2018) Autoclaving Biohazardous Waste Guidelines. https://www.ehs.washington.edu/system/files/resources/autoclave-biowaste.pdf.

172. International Organization for Standardization. (2019) ISO 35001:2019 Biorisk Management for Laboratories and other Related Orgnaisations. Switzerland: International Organization for Standardication

173. Johnson CM, Dobbs KM. (2019) The Evolving Landscape of Institutional Biosafety Committees and Biosafety Programs: Results from a National Survey on Organizational Structure, Resources, and Practices. *Appl Biosaf.* 24 (4)**:** 213-219.

174. Greene D et al. (2023) The Biorisk Management Casebook: Insights into Contemporary Practices. Standford Digital Repository. Available from: https://purl.stanford.edu/hj505vf5601.

175. U.S. National Institutes of Health. (2024) NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines). Prepared for U.S. Department of Health and Human Services. https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf.

176. World Health Organization. (2022) WHO Global Action Plan for Poliovirus Containment, 4th edition (GAP IV). Switzerland: WHO Press.

177. World Health Organization. (2010) 3 - The Biorisk Management Framework for Responsible Life Sciences Research. *Responsible Life Sciences Research for Global Health Security: A Guidance Document*. Geneva, Switzerland: WHO Press.

178. U.S. National Institutes of Health Office of Science Policy. FAQs on Institutional Biosafety Committee (IBC) Administration. https://osp.od.nih.gov/policies/biosafety-and-biosecurity-policy/faqs-on-institutional-biosafety-committee-ibc-administration-april-2024/. Last Updated May 2024. Accessed September 18, 2024.

179. European Committee for Standardiazation [CEN]. (2011) CEN Workshop Agreement (CWA) 15793: Laboratory Biorisk Management. Brussels, Belgium: CEN.

180. Gemmellaro T. Webinar - Lab Inspections vs. Audits: What's the Difference & Why Does It Matter? https://www.slideshare.net/TriumvirateEnvironmental/lab-inspections-vs-audits-whats-the-difference-why-does-it-matter#45. Accessed October 9, 2024.

181. Wolters Kluwer. Audits and Inspections: Knowing the Difference https://www.wolterskluwer.com/en/expert-insights/audits-and-inspections-knowing-the-difference#:~:text=At%20a%20high%20level%2C%20inspections%20are%20a%20%E2%80%9Cdo%E2%80%9D,including%20that%20the%20required%20inspections%20have%20been%20done. Archived: https://web.archive.org/web/20241009162800/https://www.wolterskluwer.com/en/expert-insights/audits-and-inspections-knowing-the-difference. Last Updated March 12, 2021. Accessed October 18, 2024.

182. Burnett L, Olinger P. (2015) Chapter 8: Evaluating Biorisk Management Performance. In *Biorisk Management - Biosafety and Biosecurity*. Salerno RM, Gaudioso J (eds.). Boca Raton, FL, USA: CRC Press.

183. Trucks HM. (2017) An Assessment of the Effectiveness of Unannounced Safety Inspections Versus Announced Inspections in Academic Research Laboratories That Utilize Biological Hazards. MPH Thesis, College of Public Health. Lexington, KY: University of Kentucky.

184. Qin Q et al. (2023) Best practices for implementing biosafety inspections in a clinical laboratory: Evidence from a multi-site experimental study. *PLoS One.* 18 (10)**:** e0292940.

185. Barach P, Small SD. (2000) Reporting and preventing medical mishaps: lessons from non-medical near miss reporting systems. *BMJ.* 320 (7237)**:** 759.

186. Boeing. (2023) Statistical Summary of Commercial Jet Airplane Accidents. Prepared for Boeing https://www.boeing.com/content/dam/boeing/boeingdotcom/company/about_bca/pdf/statsum.pdf.

187. Phimister JR et al. (2003) Near-Miss Incident Management in the Chemical Process Industry. *Risk Analysis.* 23 (3)**:** 445-459.

188. Vincent C, Stanhope N, Crowley-Murphy M. (1999) Reasons for not reporting adverse incidents: an empirical study. *Journal of Evaluation in Clinical Practice.* 5 (1)**:** 13-21.

189. Ritterson R, Casagrande R. (2017) Basic Scholarship in Biosafety Is Critically Needed To Reduce Risk of Laboratory Accidents. *mSphere.* 2 (2)**:** 10.1128/msphere.00010-00017.

190. Chamberlain AT et al. (2009) Biosafety Training and Incident-reporting Practices in the United States: A 2008 Survey of Biosafety Professionals. *Appl Biosaf.* 14 (3)**:** 135-143.

191. Manheim DB. (2021) Results of a 2020 Survey on Reporting Requirements and Practices for Biocontainment Laboratory Accidents. *Health Secur.* 19 (6)**:** 642-651.

192. Schröder I et al. (2016) Laboratory safety attitudes and practices: A comparison of academic, government, and industry researchers. *Journal of Chemical Health & Safety.* 23 (1)**:** 12-23.

193. Simmons HE, Matos B, Simpson SA. (2017) Analysis of injury data to improve safety and training. *Journal of Chemical Health & Safety.* 24 (1)**:** 21-28.

194. Ross E, Harper DR. (2023) Laboratory Accidents and Biocontainment Breaches - Policy Options for Improved Safety and Security. Prepared for Royal Institute of International Affairs. https://www.chathamhouse.org/sites/default/files/2023-12/2023-12-12-laboratory-accidents-biocontainment-breaches-ross-and-harper.pdf.

195. Brook OR et al. (2015) Root Cause Analysis: Learning from Adverse Safety Events. *RadioGraphics.* 35 (6)**:** 1655-1667.

196. Choucrallah D et al. (2019) Surveillance of laboratory exposures to human pathogens and toxins: Canada 2018. *Can Commun Dis Rep.* 45 (9)**:** 244-251.

197. Government of Canada. (2021) Canadian Biosafety Guideline: Incident Investigation. 87. Ottawa, ON, Canada: Public Health Agency of Canada.

198. Labconco Corporation. An Inexact Sciene: Biosafety Risk Assessment. https://www.labconco.com/articles/an-inexact-science-biosafety-risk-assessment. Archived: . Last Updated April 30, 2019. Accessed October 14, 2024.

199. Astuto-Gribble LM, Caskey SA. (2014) Laboratory Biosafety and Biosecurity Risk Assessment Technical Guidance Document. Prepared for Sandia National Lab. https://www.aam.org.ar/descarga-archivos/Laboratory-Biosafety-Biosecurity-Guidance.pdf.

200. Sinclair RG et al. (2012) Criteria for selection of surrogates used to study the fate and control of pathogens in the environment. *Appl Environ Microbiol.* 78 (6)**:** 1969-1977.

201. Layman ML, Ramsey CL, Newman SE. (2020) Potential Surrogates for Evaluation of Decontamination Methods Under Field Study Conditions or BSL-2 Biosecurity Lab Conditions: A Review. *Global Journal of Agricultural Innovation, Research & Development.* 7**:** 45-53.

202. Division of Select Agents and Toxins. Division of Agricultural Select Agents and Toxins (DASAT) Policy Statement: Personal Quarantine Policy for Specified Veterinary Services (VS) Select Agents. https://www.selectagents.gov/regulations/policy/personal-quarantine.htm. Archived: . Last Updated December 3, 2021. Accessed March 31, 2023.

203. Astuto-Gribble L, Tria E, Wallis L. (2015) Chapter 2 - The AMP Model. In *Biorisk Management: Biosafety and Biosecurity*. Salerno R, Gaudioso J (eds.). 31-42. Boca Raton, FL, USA: CRC Press.

204. Ritterson R et al. (2022) A Call for a National Agency for Biorisk Management. *Health Security.* 20 (2)**:** 187-191.

205. Greene D, Palmer MJ, Relman DA. (2023) Motivating Proactive Biorisk Management. *Health Secur.* 21 (1)**:** 46-60.

206. Perkins D et al. (2019) The Culture of Biosafety, Biosecurity, and Responsible Conduct in the Life Sciences: A Comprehensive Literature Review. *Applied Biosafety.* 24 (1)**:** 34-45.

207. Carvalho REFL et al. (2023) Factors determining safety culture in hospitals: a scoping review. *BMJ Open Qual.* 12 (4).

208. International Association of Oil & Gas Producers. (2013) Shaping Safety Culture Through Safety Leadership (OGP Report No. 452). Prepared for IOGP. https://www.iogp.org/bookstore/product/shaping-safety-culture-through-safety-leadership/.

209. Machfudiyanto RA et al. (2020) Identification of institutional safety factors affecting safety culture in construction sector in Indonesia. *IOP Conference Series: Earth and Environmental Science.* 426.

210. National Research Council. (2014) Safe Science: Promoting a Culture of Safety in Academic Chemical Research. Washington, DC, USA: The National Academies Press.

211. Task Force for Advancing the Culture of Laboratory Safety at Stanford University. (2014) Advancing Safety Culture in the University Laboratory: A Report of the Task Force for Advancing The Culture of Laboratory Safety at Stanford University. Stanford, CA, USA.

212. Ménard AD, Trant JF. (2020) A review and critique of academic lab safety research. *Nat Chem.* 12 (1)**:** 17-25.

213. Astion M. Burnout: A New Frontier in Patient Safety? https://myadlm.org/cln/articles/2013/october/burnout. Archived: https://web.archive.org/web/20250109191047/https://myadlm.org/cln/articles/2013/october/burnout. . Accessed January 9, 2025.

214. Hernandez JS. The Human Cost of Burnout and Errors in the Laboratory. https://myadlm.org/cln/articles/2018/april/the-human-cost-of-burnout-and-errors-in-the-laboratory. Archived: https://web.archive.org/web/20250109181400/https://myadlm.org/cln/articles/2018/april/the-human-cost-of-burnout-and-errors-in-the-laboratory. . Accessed January 9, 2025.

215. Ju K et al. (2024) Association of work ability with job burnout and sleep quality among biosafety laboratory personnel in Xinjiang, China: a cross-sectional study. *Front Public Health.* 12**:** 1479257.

216. Zhu K, Chen Z. (2024) A Qualitative Exploration on Psychological Stressors and Coping Mechanisms in Medical Laboratory Personnel. *Pacific International Journal.* 7 (5)**:** 44-50.

217. Herstein JJ et al. (2021) A pilot study of core body temperatures in healthcare workers wearing personal protective equipment in a high-level isolation unit. *Journal of Occupational and Environmental Hygiene.* 18 (9)**:** 430-435.

218. Williams J et al. The Physiological Burden of Prolonged PPE Use on Healthcare Workers During Long Shifts. https://blogs.cdc.gov/niosh-science-blog/2020/06/10/ppe-burden/. Archived: https://web.archive.org/web/20240731134841/https://blogs.cdc.gov/niosh-science-blog/2020/06/10/ppe-burden/. Accessed July 31, 2024.

219. Klotz L. Human Error in High-Biocontainment Labs: A Likely Pandemic Threat. https://thebulletin.org/2019/02/human-error-in-high-biocontainment-labs-a-likely-pandemic-threat/. Archived: http://web.archive.org/web/20230331131917/https://thebulletin.org/2019/02/human-error-in-high-biocontainment-labs-a-likely-pandemic-threat/. Last Updated February 25, 2019. Accessed March 31, 2023.

220. Casagrande R et al. Gryphon Scientific LLC. (2015) Risk and Benefit Analysis of Gain of Function Research. Prepared for the National Insitutes of Health, Department of Health and Human Services. http://gryphonsci.wpengine.com/wp-content/uploads/2018/12/Risk-and-Benefit-Analysis-of-Gain-of-Function-Research-Final-Report-1.pdf.

221. Occupational Safety and Health Administration. Medical Screening and Surveillance. https://www.osha.gov/medical-surveillance/surveillance. Archived: https://web.archive.org/web/20240318182602/https://www.osha.gov/medical-surveillance/surveillance. Accessed March 18, 2024.

222. Day T et al. (2006) When is quarantine a useful control strategy for emerging infectious diseases? *Am J Epidemiol.* 163 (5)**:** 479-485.

223. Homer LC et al. (2013) Guidelines for Biosafety Training Programs for Workers Assigned to BSL-3 Research Laboratories. *Biosecur Bioterror.* 11 (1)**:** 10-19.

224. U.S. National Institutes of Health Office of Human Resources. Competencies Proficiency Scale. https://hr.nih.gov/working-nih/competencies/competencies-proficiency-scale. Accessed October 15, 2024.

225. Rober K. Proficiency: Explained. https://learnexus.com/blog/proficiency/#:~:text=Measuring%20proficiency%20is%20a%20complex%20process%20as%20it,proficiency%2C%20including%20tests%2C%20observations%2C%20self-assessments%2C%20and%20performance%20evaluations. Last Updated December 2023. Accessed October 15, 2024.

226. Hall K et al. (2024) Biosafety Level 2 Training Programs at Institutions of Higher Learning in the United States. *Applied Biosafety.*

227. U.S. Centers for Disease Control and Prevention. (2024) Select Agents and Toxins. Title 42, § 73.9. Washington, DC, USA: Office of the Federal Register, National Archive and Records Administration.

228. U.S. Department of Agriculture. (2024) Possession, Use, and Transfer of Select Agents and Toxins. Title 9, § 121. Washington, DC, USA: Office of the Federal Register, National Archive and Records Administration.

229. U.S. Department of Agriculture. (2024) Possession, Use, and Transfer of Select Agents and Toxins. Title 7, § 331. Washington, DC, USA: Office of the Federal Register, National Archive and Records Administration.

230. U.S. Occupational Safety and Health Association. (2024) Bloodborne Pathogens. Title 29, § 1910.1030. Washington, DC, USA: Office of the Federal Register, National Archive and Records Administration.

231. Wiggins G, McTighe J. (1998) What is Backward Design? In *Understanding by Design*. 7-19. Alexandria, VA, USA: Association for Supervision and Curriculum Development.

232. Lane S, Raymond MR, Haladyna TM (eds). (2016) *Handbook of Test Development*. Second edn. New York, NY, USA: Routledge, Taylor & Francis Group.

233. Kaufman SG, Berkelman RL. (2007) Biosafety “Behavioral-Based” Training for High Biocontainment Laboratories: Bringing Theory into Practice for Biosafety Training. *Applied Biosafety.* 12**:** 178 - 184.

234. Koriat A, Bjork RA. (2005) Illusions of competence in monitoring one's knowledge during study. *J Exp Psychol Learn Mem Cogn.* 31 (2)**:** 187-194.