UCT Biosafety and Biosecurity

KEY CONCEPTS OF INTEGRATED BIORISK MANAGEMENT

BACKGROUND

Life sciences R&D institutions and laboratory managers must regularly evaluate and ensure the effectiveness of the Biosafety and Biosecurity programmes, the proficiency of the workers, compliance with South African and international legislation, and the capability of equipment, facilities, and management practices to provide containment and ensure the security of potentially hazardous biological agents (pHBAs). Similarly, researchers and staff who handle pHBAs must understand the containment conditions and specific requirements under which these organisms and materials should be safely handled, stored and secured. Regular Biosafety and Biosecurity compliance audits and internal facility inspections should therefore be performed.

THE IMPORTANCE OF LABORATORY BIOSAFETY AND BIOSECURITY IN LIFE SCIENCE RESEARCH ENVIRONMENTS

Life sciences research and innovation offer endless opportunities to improve human health, increase crop yields and food safety, and contribute to environmental sustainability. There are, however, risks associated with working in life sciences research laboratories. These work environments may pose infectious disease risks to people that work in and near them. The knowledge, information, products, technologies, and equipment in these laboratories may also be deliberately misapplied (e.g., dual-use research) to pose a significant biosecurity risk, including bioterrorism threats with broad potential consequences to public health and safety, agricultural crops, animals and the environment. The implementation of an **integrated biorisk management** system and a "safe culture" that promotes safe, secure, ethical and responsible practices are therefore essential.

INTEGRATED BIORISK MANAGEMENT

Laboratory biosafety, biosecurity and the **oversight of dual-use research** are the three main elements of an integrated biorisk management system.

1. **Biosafety** includes the containment principles, technologies and practices that are implemented to prevent unintentional exposure or release of potentially hazardous biological materials such as human, animal or plant pathogens and toxins, genetically modified organisms (GMOs) and human and animal biological samples.
2. The term "**laboratory biosecurity**" is used to describe the principles, technologies and practices that are implemented for the protection, control and accountability of specific biological agents and toxins and/or the equipment, skills and data related to their handling within facilities. The aim of biosecurity measures is to prevent unauthorised access, loss, theft,

misuse, diversion or intentional, unauthorised release of these pathogens and/or toxins (adapted from WHO, 2020). Important biosecurity requirements include the evaluation of the dual-use potential of the biological agents, data or knowledge created in a research project, physical security (access control and monitoring), personnel management, inventory and material accountability tracking, information or data security, material transport policies and accident, injury and incident response plans.

3. **Oversight of dual-use research.** Dual-use research of concern (DURC) is life sciences research conducted for legitimate purposes to generate knowledge, information, technologies, and/or products that could be **directly misapplied to pose a significant threat with broad potential consequences** to public health and safety, agricultural crops and other plants, animals, the environment, material, or national security. **Research oversight** increases awareness about the biosafety and biosecurity concerns associated with certain types of research to ensure that appropriate risk mitigation measures are in place to prevent biosafety and biosecurity incidents (WHO; US Government Policy for oversight of DURC and PEPP).

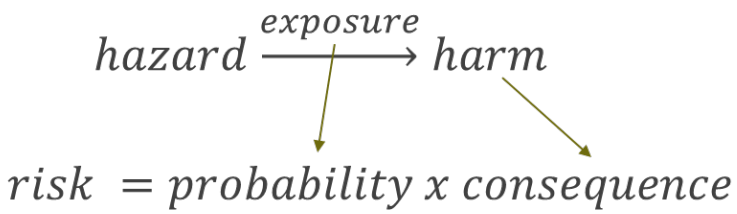
PRINCIPLES OF BIOSAFETY MANAGEMENT

The two principles of biosafety practice/management are 1) biological risk assessment within a risk analysis framework and 2) containment.

1. RISK ANALYSIS FRAMEWORK

The risk analysis framework includes the biological risk assessment, risk management and risk communication (Figure 1). The risk assessment conclusion will be used to determine the appropriate risk management and control measures and biosafety containment level.

i. **Biological risk assessment** is a systematic process – quantitative or qualitative – of gathering information and evaluating the nature and characteristics of the hazard (infectious or potentially infectious biological agent), determining the probability of exposure to the hazard (considering the characteristics of the hazard and specific laboratory procedures/ activities) and the magnitude of potential harm (consequences) caused by exposure to the hazard.



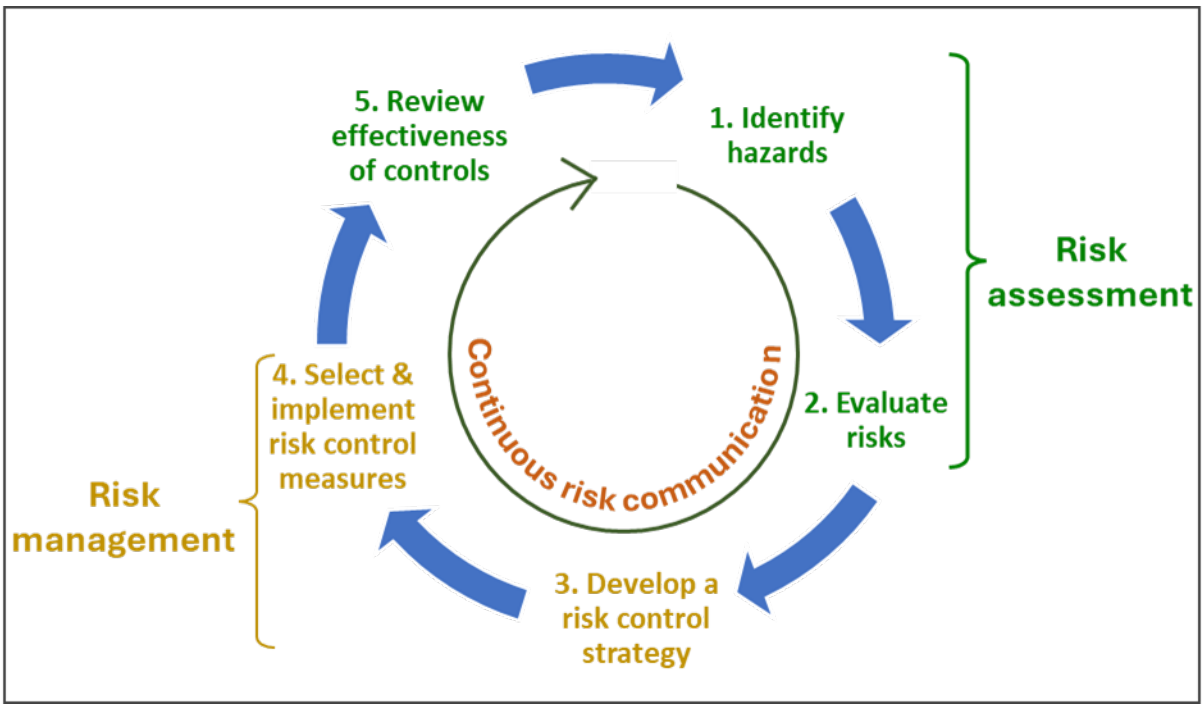


Figure 1. Biological risk assessment process (Adapted from CDC, 2021)

All potentially hazardous biological agents (pHBAs) including any microorganisms, toxins, cell or organic material of plant, human or animal origin, including any which have been genetically modified, which may cause infection, allergy or toxicity should be considered. Pathogenic biological agents are classified into four hazard groups (Table 1) according to the level of risks to humans by the Advisory Committee on Dangerous Pathogens (ACDP). Specified animal pathogens are also categorized into four groups.

Table 1. Classification of biological agents according to level of risk of infection to humans

Increasing risk ↓	Human pathogen hazard group	Level of risk of infection to humans
	Group 1	Unlikely to cause human disease by infection or toxicity.
	Group 2	Can cause human disease, may be a hazard to employees, unlikely to spread to the community, effective prophylaxis or treatment available.
	Group 3	Can cause severe human disease, may be a serious hazard to employees, may spread to the community, usually effective prophylaxis or treatment available.
	Group 4	Causes severe human disease, serious hazard to employees, likely to spread to the community, usually no effective prophylaxis or treatment available.

ACDP Approved List 2023: https://www.hse.gov.uk/pubns/misc208.pdf

ii. **Risk management or control** is the identification and implementation of technologies, biosafety containment measures or practices (see point 2 below) that should be used or followed to avoid or minimise the likelihood or impact of exposure (risk mitigation). The **hierarchy of controls** (Figure 2) is a method of identifying and ranking safeguards to protect workers from hazards. The outcome of the risk assessment will assign an appropriate biosafety level to the work, that will dictate the appropriate physical barriers, biosafety cabinets, appropriate personal protective equipment (PPE) and response to accidents or spills. The continued monitoring of risks, reporting of incidents and laboratory-acquired infections, and updating risk management strategies are of utmost importance.

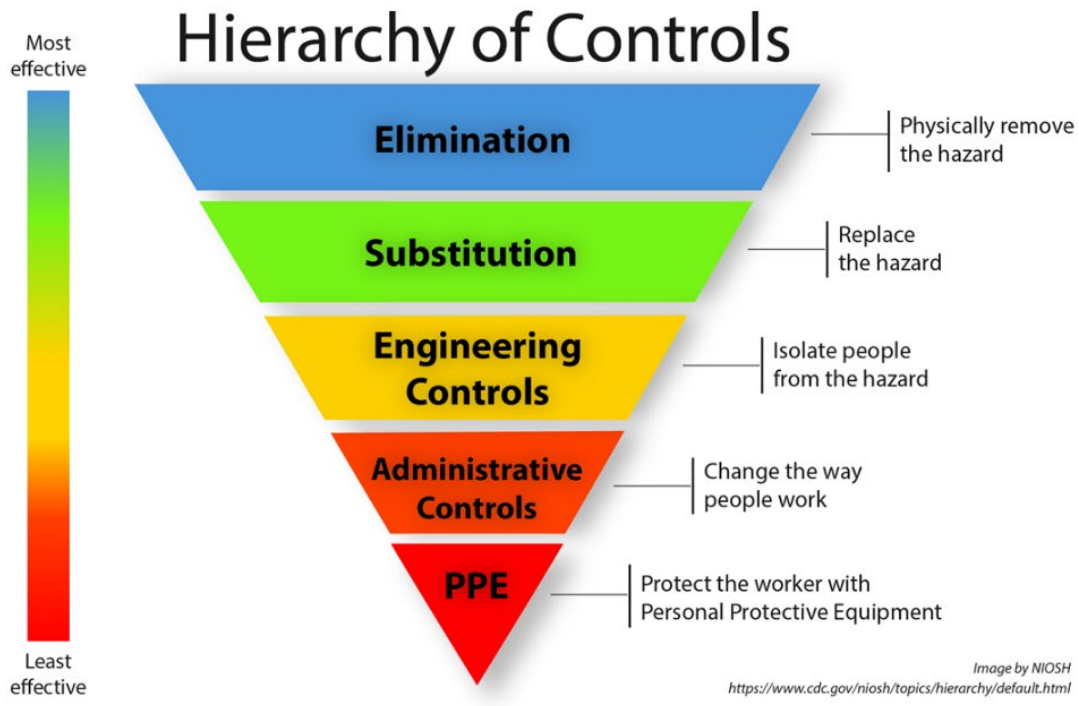


Figure 2. The hierarchy of biosafety controls included in a risk management strategy.

iii. **Risk communication** includes the training of researchers, the development of standard operating procedures (SOPs) to guide the safe handling and disposal of the specific biological agent, signage (OH&S aspects), reporting of incidents, etc.

Education and practical training of all individuals involved in activities with biological agents is an important responsibility and prerequisite for the effective management of biosafety and biosecurity risks. Training programmes must be designed to provide the necessary knowledge and skills for the safe handling, storage and transport of biological

materials, treatment of biological waste, correct operation of equipment, and the prevention of accidents and incidents.

2. CONTAINMENT

Includes microbiological practices, controls, safety- and personal protective equipment, and facility and infrastructural safeguards that protect laboratory workers, the environment, and the public from exposure to infectious microorganisms, toxins and biological materials (biorisks) that are handled and stored in the laboratory.

Four ascending risk categories or levels of containment, referred to as **Biosafety Levels** 1 through 4 (Figure 3), are defined by the primary risk criteria of infectivity, severity of disease, transmissibility, and the nature of the work being conducted (CDC). Each Biosafety level describes the containment measures, practices, primary and secondary barriers including PPE for the corresponding level of risk associated with handling a specific biological agent during specific procedures (Table 2). Risk control measures range from **core measures** (BSL-1), and **heightened measures** (BSL-2 and BSL-3) to **maximum control measures** (BSL-4) (WHO, 2020).

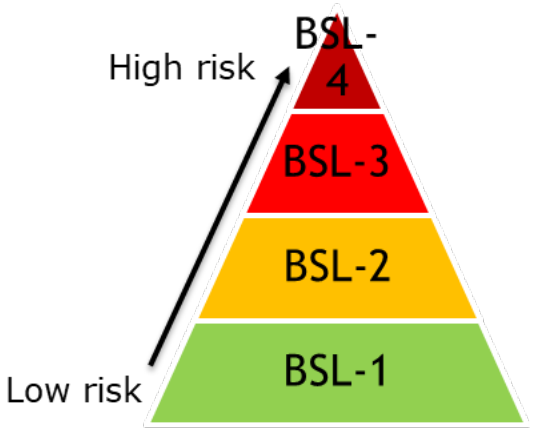


Figure 3. Four Biosafety levels defined by the primary risk criteria of biological agent infectivity, severity of disease, transmissibility, and the nature of the work being conducted.

- **Core requirements:** Set of minimum requirements, a combination of risk control measures that are both the foundation for and an integral part of laboratory biosafety. Reflect international standards & best practice in biosafety -necessary to work safely with biological agents, even where the associated risks are minimal.
- **Heightened control measures:** The outcome of a risk assessment indicates that the biological agents being handled &/or the activities to be performed with them are associated with a risk that cannot be brought to an acceptable risk with the core requirements only.
- **Maximum containment measures:** A set of highly detailed and stringent risk control measures necessary during laboratory work where a risk assessment indicates that the activities to be performed pose very high risks to laboratory personnel, the wider community &/or the environment

Biosafety level ≠ Hazard or risk group of a biological agent

Table 2. Summary of recommended biosafety controls for the four Biosafety levels (BSL)

BSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	▪ No primary barriers required. ▪ PPE: laboratory coats and gloves; eye, face protection, as needed	Laboratory bench and sink required
2	▪ Agents associated with human disease ▪ Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: ▪ Limited access ▪ Biohazard warning signs ▪ "Sharps" precautions ▪ Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: ▪ BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials ▪ PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus: ▪ Autoclave available
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure	BSL-2 practice plus: ▪ Controlled access ▪ Decontamination of all waste ▪ Decontamination of laboratory clothing before laundering	Primary barriers: ▪ BSCs or other physical containment devices used for all open manipulations of agents ▪ PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed	BSL-2 plus: ▪ Physical separation from access corridors ▪ Self-closing, double-door access ▪ Exhausted air not recirculated ▪ Negative airflow into laboratory ▪ Entry through airlock or anteroom ▪ Hand washing sink near laboratory exit
4	▪ Dangerous/exotic agents which post high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments ▪ Agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level ▪ Related agents with unknown risk of transmission	BSL-3 practices plus: ▪ Clothing change before entering ▪ Shower on exit ▪ All material decontaminated on exit from facility	Primary barriers: ▪ All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit	BSL-3 plus: ▪ Separate building or isolated zone ▪ Dedicated supply and exhaust, vacuum, and decontamination systems ▪ Other requirements outlined in the text

From CDC Lab training: https://www.cdc.gov/labtraining

Biosafety controls are biosafety level-specific and include primary, secondary and tertiary containment barriers.

- Primary containment barriers directly at the level of the hazard: Safety equipment (Biological safety cabinet (BSC), enclosed containers and animal caging systems, puncture-proof sharps container, specific PPE.
- Secondary containment barriers: Infrastructure surrounding primary barriers (facility design, access control, directional airflow, HEPA filters, autoclave, etc.).
- Tertiary containment: Environment beyond containment laboratory.

BIOSAFETY AND BIOSECURITY RESOURCES

UCT research staff and students can access relevant Biosafety and Biosecurity resources on the OHSE Biosafety website:
https://uct.ac.za/staff/biosafety#:~:text=The%20term%20%E2%80%9Claboratory%20biosecurity%E2%80%9D%20is,to%20their%20handling%20within%20facilities

KEY DEFINITIONS

Accidental pathogen escape from laboratory settings (APELS): Unintended movement of a laboratory pathogen to the outside environment following a breach of biocontainment caused by procedural or engineering failures. Internal or external pathogen release.
Biological agent: A microorganism, virus, biological toxin, particle or otherwise infectious material, either naturally occurring or genetically modified, which may have the potential to cause infection, allergy, toxicity or otherwise create a hazard to humans, nonhuman animals or plants (WHO).
Biological risk assessment: A systematic process – quantitative or qualitative – of gathering information and evaluating the nature and characteristics of the hazard (infectious or potentially infectious biological agent), determining the probability of exposure to the hazard (considering the specific laboratory procedures/ activities) and the magnitude of potential harm (consequences) caused by exposure to the hazard.
Biorisk: A combination of the probability of occurrence of harm and the severity of that harm where the source of harm is a biological agent or toxin (CWA 15793). The source of harm may be unintentional exposure, accidental release or loss, theft, misuse, diversion, unauthorized access or intentional unauthorized release. Biorisks include both biosafety and biosecurity risks.
Biorisk management: The analysis of ways and development of strategies to minimize the likelihood of the occurrence of biorisks. The management of biorisk places responsibility on the facility and its manager to demonstrate that appropriate and valid biorisk reduction (minimisation) procedures have been established and are implemented. Integrated biorisk management includes biosafety, biosecurity and oversight of dual-use research (WHO, 2022)
Biosafety levels: A standard set of biocontainment or safety precautions or controls required to contain potentially hazardous biological agents and keep laboratory workers safe when handling these biological agents and specific equipment. The levels of containment range from the lowest biosafety level 1 (BSL-1) to the highest at level 4 (BSL-4) and each level builds on the controls of the level before it. All the levels follow standard microbiological practices (including not eating, drinking, or applying cosmetics, washing hands after working in the lab, routinely decontaminating the work area, etc.).
Dual-use research: Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, material, or national security. Also referred to as dual-use research of concern (DURC).

Hazard: Biological agents that have the potential to cause adverse effects (harm) to personnel and/or humans, animals, and the wider community and environment. A hazard ≠ risk (see definition of "risk" below).
Laboratory-acquired or laboratory-associated infections (LAI): Any infection acquired or reasonably assumed to be acquired by exposure to a biological agent during laboratory-related activities.
Laboratory biosafety: Containment principles, technologies and practices that are implemented to prevent unintentional exposure or release of potentially hazardous biological materials such as human, animal or plant pathogens and toxins, genetically modified organisms (GMOs) and human and animal biological samples. Principles of biosafety include biological risk assessment and containment.
Laboratory biosecurity: Principles, technologies and practices that are implemented for the protection, control and accountability of specific biological agents and toxins and/or the equipment, skills and data related to their handling within facilities. To prevent the unauthorised access, loss, theft, misuse, diversion, sabotage or intentional misuse and release of these biological agents (pathogens and/or toxins), equipment or information.
Risk: The combination of the probability that a hazard will cause harm and the severity of harm that may arise from exposure to that hazard. Risk = probability of exposure x consequence of exposure.
Risk management: Identification and implementation of appropriate technologies, biosafety measures, controls or practices to avoid or minimise the likelihood or impact of the exposure (risk mitigation). Assigning an appropriate BSL, monitoring risks, reporting incidents and laboratory-acquired infections, and updating risk management strategies.
Zoonotic agents/Zoonoses: Biological agents originating from animals or from products of animal origin which can cause disease in humans. A zoonotic disease is a disease that can naturally be transmitted from vertebrate animals to humans or vice versa.