BIORISK MANAGEMENT STANDARD FOR LARGE-SCALE WORK INVOLVING BIOLOGICAL AGENTS

Draft as on 31 Mar 2024

MOH Biosafety Branch
MOH_BioSafety@moh.gov.sg

Contents

1 FOREWORD

The Biorisk Management Standard for Large-Scale Work involving Biological Agents (henceforth, referred to as the standard) has been developed by the Ministry of Health Biosafety Branch with advice from an Expert Panel.

The standard is developed to assist organisations in establishing a framework that supports safe and secure operations involving large-scale production and/or manipulation of **pathogenic** biological agents for research, manufacturing, or other purposes.

The standard builds on the principles outlined in the International Organization Standardization document for Biorisk management for laboratories and other related organisation (ISO 35001). It draws reference from local legislations and standards, as well as international guidelines, including the Singapore Biological Agents and Toxins Act (BATA), the Singapore Standard Specifications for high containment (biosafety level 3) facility (SS 696:2023), the Fourth Edition of World Health Organization Global Action Plan for Poliovirus Containment (WHO GAP IV), the Fourth Edition of WHO Laboratory Biosafety Manual (WHO LBM), and the Sixth Edition of United States Centers for Disease Control and Prevention Biosafety in Microbiological and Biomedical Laboratories (BMBL).

While the standard advocates a risk-based management approach, centred on biosafety and biosecurity (biorisk), organisations are advised to adopt the “all-hazard approach” and develop a holistic framework covering all aspects of risk without compromising the overall biorisk management framework, while complying with the relevant legislative requirements.

2 ABBREVIATIONS AND DEFINITIONS

2.1 Abbreviations

BATA	Biological Agents and Toxins Act (Singapore)
BMBL	Biosafety in Microbiological and Biomedical Laboratories (Sixth Edition, United States Centers for Diseases Control)
BRM	Biorisk Management
BSC	Biosafety Cabinet
BSL	Biosafety Level
EDS	Effluent Decontamination System
GM	Genetically Modified
GMP	Good Manufacturing Practice
GMPP	Good Microbiological Practices and Procedures
HEPA	High Efficiency Particulate Air
LBM	Laboratory Biosafety Manual (Fourth Edition, World Health Organization)
NIH	National Institute of Health
OHP	Occupational Health Programme
PPE	Personal Protective Equipment
RG	Risk Group or Risk Grouping
SOP	Standard Operating Procedure
SS 696:2023	Singapore Standard: Specification for High Containment (Biosafety Level 3) Facility

2.2 Definitions

Terms	**Description**
Accident	An unplanned or unintended event that results in injury or damage.
Aerosol	Small liquid or solid particles (with a size less than 100 micrometres in diameter) suspended in air that can potentially be inhaled into the respiratory tract.
Airlock	A vestibule that serves as a controlled entry and exit point, with two interlocking doors (hard-interlocked airtight door assemblies) to prevent undesirable airflow from one area to another.

Anteroom	A vestibule that serves as a controlled entry and exit point, with two interlocking doors (via hard- or soft- interlocked door assemblies) to manage airflow, either as a bubble (where the anteroom is positive to adjoining spaces), sink (where the anteroom is negative to adjoining spaces), or cascade (higher pressure exists on one side of the anteroom, which transitions to lower pressure in another adjacent space). *Refer to Figure A1 in Annex A for the different designs.*
Audit	A procedure to systematically evaluate records, activities or processes to ensure compliance and effectiveness.
Backdraft protection	Ventilation system or strategies to prevent air reversal and prevent contaminating the supply air. Such system or strategies must be validated.
Backflow preventer	Devices installed onto a pipe that only allow water to flow in one direction, preventing reversal and contamination of the source.
Biohazard	Biological substances, materials, or microorganisms that pose a risk to the health and safety of living organisms.
Biological agent	Any microbiological entity, cellular or non-cellular, naturally occurring or engineered, capable of replication or of transferring genetic material that may be able to provoke infection, allergy, toxicity or other adverse effects in humans.
Biological material	Any substance containing components of living microorganisms or *biological agents*, which is used for purposes such as medical, therapeutic, diagnostic or research. Such materials may include vaccines, gene therapies, clinical samples including blood components and tissues, etc.
Bioreactor	A device, apparatus or vessel that facilitate the growth of *biological agents* or biological mass through the transformation of degradation of materials fed to the reactor. It is a type of *primary containment device*.
Biorisk	A combination of the probability of an occurrence of harm and the severity of that harm where source of harm is a *biological agent* or *biological material*. The harm can be the consequence of an unintentional exposure, accidental release, or loss, theft, misuse, diversion, unauthorised access, or intentional unauthorised release. Biorisk shall encompass both *biosafety* and *biosecurity* risks.
Biorisk management committee	Organisational or institutional representatives with diverse backgrounds, expertise and competency in managing *biorisk*.

Biorisk management system	The organisation structure, planning activities, responsibilities, practices, procedures, processes, and resources for developing, implementing, achieving, reviewing, and maintaining an organisation's *biorisk* policy and its objective.
Biosafety	Practices, technologies and strategies pertaining to the principle of *containment*, implemented to prevent accidental release or unintentional exposure of *biological agents* or *biological materials.*
Biosafety cabinet	A type of *primary containment device* which is commonly used in biological laboratories to provide personal and environmental protection, and with additional protection to product for the higher classes of biosafety cabinet.
Biosecurity	Practices, technologies and strategies, implemented for the protection, control and accountability of *biological agents* or *biological materials* and to prevent unauthorised access, loss, theft, misuse, and diversion, or their intentional release.
Closed system	A validated system which provides a complete physical barrier between biological material and personnel.
Containment	The combination of physical design parameters and operational practices that protects personnel, the immediate work environment, and the community from exposure to hazardous *biological agents* or hazardous *biological materials*. The term "biocontainment" is also used in this context.
Containment area	Also called contained area. It is an area dedicated to handle or store hazardous *biological agents* or hazardous *biological materials*, where physical parameters and operating practices are integrated to protect *workers*, work environment and the community. Containment area is typically considered as "potentially contaminated" and is maintained with inward directional airflow to ensure hazardous *biological agents* and hazardous biological materials are "kept-within".
Containment perimeter	Boundary that separates *containment area* from its adjacent external (outside) area, i.e. the non-containment area.
Decontamination	Process which renders hazardous *biological agents* or hazardous *biological materials* safe to handle and unlikely to cause infection, and is typically accomplished via *disinfection*, *sterilisation* or *fumigation*.
Disinfection	A process to reduce the number of living microorganisms, but not bacteria spores, without necessarily killing or removing all microorganisms to prevent infection.

Effluent decontamination system	Also known as liquid waste treatment system. It refers to a system comprising of equipment or installation integrated within or connected to the drainage or plumbing that is used to decontaminate, through heat or chemical means or both the liquid waste (i.e. effluent) produced in a *containment area* prior to release into sanitary sewers.
Emergency shower	The means by which to flush all or part of the body with copious amounts of water to minimise the harmful effects of chemicals or other hazardous substances when splashed or spattered onto the skin.
Facility	An operational unit and associated buildings and equipment used to manage *biological agents* or *biological materials.* This includes the *laboratory*, together with the supporting infrastructure, equipment, and services, including ancillary rooms, such as *airlocks*, *anterooms*, changing rooms, sterilising rooms, and storage rooms.
Incident	Event with a potential for causing harm. An *accident* is an incident which has resulted in harm, while an incident where no harm is caused is referred to as a "near miss", "near hit", "close call" or "dangerous occurrence".
Fumigation	The process whereby one or more chemicals are applied in the gaseous or vapourised state to an enclosed space for purpose of decontaminating the area and the items therein.
High efficiency particulate air filter	A filter capable of removing at least 99.97% of all particles with a mean aerodynamic diameter of 0.3 micrometres, and is certifiable to ISO 29463, EN 1822 or equivalent standards.
Isolator	A fully enclosed *primary containment* device that prevents the air within it from mixing with the room air. It contains a dedicated HEPA filter within its supply and exhaust outlets.
Laboratory	A room or clearly defined area within a *facility* designated for work involving *biological agents* or *biological materials.*
Management	The person or group of people who operates, manages, or have control of the *organisation*.
Organisation	Person or group of people who has its own functions with responsibilities, authorities, and relationships to achieve its objectives. It includes, but is not limited to, company, corporation, enterprise, partnership, institution or facility, or part or combination thereof, whether incorporated or not, public or private.

Primary containment device or equipment	Apparatus or equipment which is designed to prevent the release of *biological agents* or *biological materials* and to provide primary containment (i.e. barrier between the individual and/or the work environment and the *biological agents* or *biological materials*). Examples of primary containment devices or equipment include *bioreactors*, *biological safety cabinets*, *isolators* and centrifuges with sealable cups or rotors. All primary containment device or equipment must be validated.
Reliability	The quality of being trustworthy and lacking malicious intent.
Sterilisation	The process of eliminating or destroying all forms of microbial life, including bacteria, viruses, fungi, and spores.
Threat	An individual or group of people who has the motive, means, and opportunity to intentionally cause harm to individuals, assets, a system, an *organization*, or the environment.
Top management	The person or group of people who directs and controls an *organisation* at the highest level, and may include Chief Executive Officer, Chief Operating Officer, etc.
Vestibule	An architectural space which serves as a transitional room between exterior and interior or between rooms of differing uses, quality or classification.
Worker	Person performing work or work-related activities under the control of the *facility*.

3 INTRODUCTION

3.1 Biological Agent and Biosafety Containment Level

Biological agent

3.1.1 Biological agents are categorised into four Risk Groups (RG), namely RG1 to RG4, based on their impact on public health and safety. The risk grouping is determined according to the biological agent's trait such as its pathogenicity, transmissibility, and the availability of preventive measures and treatment regimes. RG1 biological agents are non-pathogenic and do not cause disease in healthy adult human. In contrast, RG2 to RG4 biological agents are pathogenic, with higher RGs generally associated with greater severity or higher consequences of infection.

3.1.2 While RG is a common classification for biological agents in many countries, Singapore's Biological Agents and Toxins Act (BATA) uses the term "Schedule" to differentiate the risk level of pathogenic biological agents (Table 1).

Table 1: Biological agents' risk classification by countries/region. Refer to Annex B for more details.

Classification		**Risk Level**			
Country/region	**Terminology**	**Low**	**Moderate**	**High**	**Very High**
Australia and New Zealand (Standard)	Risk Group	RG1	RG2	RG3	RG4
European Union (Directive)	Group (Grp)	Grp 1	Grp 2	Grp 3	Grp 4
Canada (Biosafety Standard)	Risk Group	RG1	RG2	RG3	RG4
United States (NIH Guidelines*)	Risk Group	RG1	RG2	RG3	RG4
Singapore (BATA)	**Schedule**	**Nil**	**Fourth Schedule**	**First Schedule**	**Second Schedule**

* Refers to NIH Guideline for Research involving Recombinant or Synthetic Nucleic Acid Molecules (2019). Department of Health and Human Services, National Institute of Health.

Biosafety containment level

3.1.3 Facilities or laboratories working with biological agents can be categorised into four containment or biosafety levels (BSLs), each with its set of containment requirements for facility and laboratory design, infrastructure, safety equipment, practices and procedures. The containment measures progressively increase from BSL1 to BSL4, with BSL4 being the highest and requires the most stringent biorisk control measures. Detailed containment measures for BSL1 to BSL4 can be found in the Sixth Edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL).

3.1.4 While in many cases, the BSL of a facility or laboratory corresponds to the RG or classification of the biological agent being worked on, this is not always the case, as risk is not solely determined by the RG or the inherent risk of the biological agent. Additional

factors such as concentration (or titre) and volume of the biological agent, the nature of activities undertaken, the safety equipment utilised and the competency of personnel, among other considerations, can influence the risk level and the containment requirements.

3.2 Large-Scale Manipulation of Biological Agent

3.2.1 Working with large volumes or high titre of biological agents can significantly increase risks. Laboratory-acquired infections attributed to aerosol exposure and inhalation have been reported in work involving high load of blood- and vector-borne viruses including human immunodeficiency virus, Chikungunya virus and Japanese encephalitis virus (Pedrosa and Cardoso, 2011). Responding to and containing spillages or accidental release of high volume or high titre biological agents can be challenging and pose a heightened risk of personal exposure. If such events occur, they can have significant negative impacts to public health and lead to reputational and economic losses for the organisation and the country.

3.2.2 Various definitions of “large scale” exist in the context of the manipulation or production of biological agents. The United States NIH Guidelines (2019) considers 10 litres or more as large scale, while the Japanese Ministry of Health defines quantities exceeding 20 litres as large scale. The BMBL (2020) and the Advisory Committee on Dangerous Pathogens (United Kingdom) however, do not define any specific quantity but rather describe large scale as volume or concentration of biological agents exceeding those typically used for general laboratory diagnosis or basic research, or as determined by the intent of the work, respectively.

3.2.3 While the Singapore BATA legislatively regulates large-scale production as work involving the production of biological agents at a quantity of 10 litres or more at any one time. It is important to emphasise that the risks of the work shall not be solely based on the volume of the biological agents. Instead, a comprehensive risk assessment shall be conducted, taking into consideration of other factors such as titre of the biological agents, activities undertaken, workers’ competency and any other workplace-associated risks (see Section 5). This is to devise a biorisk management (BRM) programme that commensurate with the risks identified to protect the workers, the community and the environment.

3.3 Purpose of the Standard

3.3.1 This standard serves as a BRM guidance document for organisations engaged in large-scale production or large-scale manipulation of **pathogenic** or **potentially pathogenic** biological agents, for vaccine research, development, manufacturing or any other related activities, to ensure compliance with the BATA requirements.

3.3.2 This standard provides requirements and guidance on the approach to establishing and maintaining an effective BRM system, with the goal of creating a safe and secure working environment and continual improvement.

3.4 Use of the Standard

3.4.1 In this standard, the following terms are used:

(a) “shall” indicates that the specification is strictly to be followed in order to conform to the standard unless it is determined to be inapplicable, and in this case, valid justifications must be provided and documented;

(b) “should” indicates a recommendation;

(c) “may” indicates a permission; and

(d) “can” indicates a possibility or capacity.

3.4.2 While care is taken to ensure the information contained herein is based on current scientific knowledge and industry best practices, it is important to note that the information provided here is not exhaustive. Organisations are advised to consult with the relevant authorities for areas that are not covered or detailed in this standard, which include the following aspects:

(a) good manufacturing practice (GMP), which are principles and requirements applicable to the manufacturing of regulated health and therapeutic products, or precursors of therapeutic products;

(b) environmental control and management of non-biological hazards such as chemical, mechanical, electrical, ergonomic and physical hazard; and

(c) handling of animals and/or biological agents that are only pathogenic to animals.

3.4.3 Organisations are responsible to ensure all legal and other requirements (e.g. standards, codes of conduct, codes of practice, guidelines, etc.) are identified and met with adequate evidence of effective integration into the BRM system, whenever applicable.

3.4.4 Organisations manufacturing biological agents and supplied as health or therapeutic products, or precursors of therapeutic products should also comply with the GMP requirements specified by the regulatory authority, in addition to biosafety and biosecurity requirements. The BRM requirements may be integrated within the GMP scheme or as a stand-alone entity. Where integration occurs, the BRM requirements shall be readily identifiable within the GMP scheme and capable of subjecting to BRM audits.

3.4.5 This standard shall be used in conjunction with other containment guidance, standards and legislations, whenever applicable.

3.4.6 References and links provided are valid as of the date of publication of this standard. Organisations are to verify the status of the cited sources to ensure the information remains relevant, current and aligns with the other requirements or standards outlined.

4. BIORISK MANAGEMENT SYSTEM

4.1 Biorisk Management System

4.1.1 An effective BRM system is critical for ensuring biosafety and biosecurity in facilities handling pathogenic biological agents or hazardous biological materials (henceforth, hazardous biological agents or materials). It is a systematic process that enables an organisation to identify, assess, control, and evaluate the biorisk inherent in its activities. An effective BRM system can protect workers’ safety and health, and prevent unauthorised access, loss, theft, diversion, or misuse of hazardous biological agents or materials and associated data or knowledge.

4.1.2 A BRM system shall include the following elements, integrating both biosafety and biosecurity risk mitigation measures.

Section	Element
5	Risk assessment and control
6	Occupational health programme
7	Personnel competence and training programme
8	Good microbiological practices and procedures
9	Personal protective equipment
10	Security programme
11	Facility physical requirements
12	Equipment and maintenance
13	Biological agents and biological materials inventory and accountability
14	Watse management, decontamination, disinfection and sterilisation
15	Emergency response and contingency plan
16	Incident, non-conformity and non-compliance management programme

4.1.3 The organisation shall establish, document, implement and maintain a BRM system in accordance with recognised standards, guidelines and industry good practices while ensuring compliance with national legislative requirements, and aligning with organisational policies related to health, safety, security, and overall business management processes.

4.2 Biorisk Management Policy

4.2.1 A BRM policy shall be established in accordance with the organisation's overarching health, safety, security and environmental framework, to either complement the existing framework or be integrated within.

4.2.2 The BRM policy shall clearly state the organisation's overall BRM objective and top management's commitment to enhancing BRM performance.

4.2.3 The BRM policy shall require that all projects/work and the related areas be assessed for risk, and a full assessment be prepared before approval is granted to commence work.

4.2.4 The BRM policy shall be appropriate to the nature and the scale of the biorisk associated with the organisation and its activities, and shall include the following aspects:

(a) safeguarding personnel (workers, contractors, visitors, community) from exposure to hazardous biological agents and materials that are stored or handled within the facility;

(b) preventing unintentional release of hazardous biological agents and materials;

(c) minimising the risk of unauthorised access and release of hazardous biological agents and materials;

(d) complying with all regulatory requirements pertaining to the handling or possessing of hazardous biological agents and materials;

(e) effectively communicating individual responsibilities and obligations regarding biorisk to all personnel, workers and relevant third parties;

(f) conducting risk assessment and implementing the required risk control measures; and

(g) continuously improving the performance of the BRM system.

4.2.5 The management is responsible for determining, implementing and maintaining the objectives and targets to achieve an effective BRM system, and establish strategies and enact procedures to monitor them. The strategies may involve regular audits or other routine checks, followed by investigation, corrective action, and reporting processes for problems identified, and ensuring adequate resources are provided to maintain the effectiveness of the strategies.

4.3 Biorisk Management Review

4.3.1 The management shall conduct periodic reviews on the BRM system at planned intervals (at least biennially as required under the BATA) to ensure its continued suitability, adequacy and effectiveness. The BRM system shall be reviewed against the requirements outlined in this standard, with deviations documented and corrective actions recorded.

4.3.2 The review process should include assessing opportunities for BRM performance improvement and determining the need to enhance systems, procedures, policies and objectives. Examples of areas for review include verification of compliance with standard operating procedures (SOPs) and work instructions, training programmes and their effectiveness, status of risk assessment activities and the effectiveness of the control strategies implemented, changes that can affect the BRM system, non-compliance or incident investigations, and status of the preventive and corrective actions.

4.3.3 The outcome of the review, together with corrective actions (including resource needs and performance indicators) shall be documented and records are maintained.

4.4 Roles, Responsibilities and Authorities

Top management

4.4.1 Top management shall hold the ultimate responsibility for the organisations or facility's BRM system but may delegate the duties and/or assign roles to competent personnel or committees with the relevant expertise and competencies. Top management however shall ensure that:

(a) appropriate measures are in place to prevent any potential conflict of interests in the delegation of the duties and roles;

(b) the BRM roles, responsibilities and delegations within the organisation are clearly defined, properly documented, and effectively communicated to all relevant parties involved; and

(c) resources are allocated to support the implementation of the BRM system.

Biorisk management committee

4.4.2 Top management shall establish a BRM committee to act as an independent committee to support the development, implementation, and management of all biorisk issues associated with the facility.

4.4.3 The BRM committee should comprise scientific and BRM advisor, biosafety, laboratory scientific and technical personnel, facility and equipment personnel, occupational health professional, security personnel, management representative, and any other relevant subject matter experts. Refer to Annex D of Singapore Standard Specification for high containment (biosafety level 3) facility (SS 696:2023) for example of the composition of BRM committee.

4.4.4 The terms of reference and functions of the BRM committee shall be clearly defined and communicated. The function of the BRM committee shall include:

(a) contributing towards the development of the organisation's BRM policies, programmes, codes of conduct and codes of practice;

(b) reviewing and approving proposals of new work or proposed modifications to existing work or activities that may have impact on BRM;

(c) reviewing and approving risk assessments, biorisk mitigation measures and protocols for work involving hazardous biological agents and materials;

(d) reviewing information related to significant incidents and data trends related to BRM performance; and

(e) reviewing and approving annual BRM plan which outlines the organisation's goals, activities and performance targets.

4.4.5 The BRM committee shall meet at regular intervals (i.e. at least half-yearly) and shall maintain records of meeting, decisions and comments from the review activities undertaken.

Occupational health professional

4.4.6 The organisation shall establish an occupational health programme (OHP) that commensurate with the facility's activities and risks.

4.4.7 A designated occupational health professional shall be appointed to support the programme. This individual shall be a medical doctor and works with the management to assess and manage risks to the worker, including advising on first aid or emergency treatment measures, and coordinating medical examinations, surveillance and vaccination programmes. Refer to Section 6 for more details on OHP.

Biosafety manager

4.4.8 A biosafety manager (officer or coordinator) who is competent in biosafety shall be appointed with operational responsibility to implement/oversee the BRM system. An alternate shall be designated in case the biosafety manager is unable to fulfil his/her responsibilities.

Security manager

4.4.9 A security manager shall be appointed and be responsible for the security requirements of the facility. The individual shall have knowledge of laboratory and facility security and liaises with others, including the biosafety manager and facility manager to implement an effective facility security programme.

Facility and equipment manager

4.4.10 One or more personnel shall be appointed with responsibilities to oversee the facility systems and equipment therein. The individual shall be an engineer or a person with adequate knowledge in containment equipment, facilities and buildings, and liaise with the biosafety manager and the security manager to assess and manage risk from the perspectives of facility and equipment, and to coordinate maintenance, building work and associated contractors.

Emergency response manager

4.4.11 One or more personnel shall be appointed to develop and implement emergency response plan and, to train and lead emergency response procedures. The individual shall have sufficient knowledge and experience in the facility infrastructure to coordinate and respond to emergency situations. This individual should liaise with other relevant facility personnel (e.g. biosafety manager, security manager, facility manager, company certified emergency team, facility emergency response team) and external emergency agencies (e.g. police, Singapore Civil Defence Forces), for emergency and contingency planning and preparedness. Refer to Section 15 for more details on emergency response and contingency planning and readiness.

Contractors and suppliers

4.4.12 Contractors and suppliers should be evaluated and selected based on their competency and awareness, compliance, and provision of products and services in line with the BRM requirements of the facility and the relevant specifications of this standard. Examples of products and services include:

(a) cleaning services;

(b) waste management or disposal services;

(c) information technology support services;

(d) equipment and facility maintenance or certification services; and

(e) security services.

4.4.13 Criteria for evaluation and selection of contractors and suppliers should be established.

4.4.14 Evaluation results and necessary actions arising from the evaluation should be documented and records retained.

4.5 Records, Documents and Data Control

4.5.1 Records, documents and data are created, controlled and retained to demonstrate compliance with the applicable requirements. These shall be legible, readily identifiable and easily retrievable.

4.5.2 All documented records (in paper or electronic form) shall be maintained for a minimum of five years. Controlled documents may include but are not limited to:

(a) SOPs and BRM manuals;

(b) job/task hazard analyses and charts of authority;

(c) facility design and commissioning records, maintenance plans and records, facility certification and/or audit reports and their associated data or findings;

(d) biorisk assessment records;

(e) medical and personal records;

(f) training records;

(g) incident reports and corrective action records;

(h) evaluation records of suppliers and contractors;

(i) containment equipment commissioning, certification, services and maintenance plans, records and reports; and

(j) inventory and transfer records of hazardous biological agents and materials.

4.6 Change Management

4.6.1 All changes associated with the design, operation and maintenance of the facility shall be subjected to a defined and documented change management process.

4.6.2 All changes shall be reviewed, verified and validated as appropriate and approved by the BRM committee before implementation. This shall include an evaluation of the effect of the changes on the risk assessment and any significant changes in risk shall be escalated to the management as appropriate. These shall be recorded as controlled documents. Examples of changes that should be subjected to the change management process include:

(a) modifications to buildings and equipment or their operation, if there is impact on BRM;

(b) changes to the programmed work, including changes to the hazardous biological agent or material used, volume, workflow or personnel;

(c) alterations to SOPs, including significant changes in materials and reagents;

(d) modification to entry/exit procedures;

(e) modification to personnel policies and visitor protocols;

(f) modifications to disinfectant, decontamination and other waste management methodologies;

(g) changes associated with the provision and use of personal protective equipment (PPE); and

(h) significant changes to goods, services, contractors or suppliers.

4.7 Communication

4.7.1 The organisation shall implement mechanisms to ensure relevant information that may affect personal operations and/or safety is defined, documented and communicated effectively to the relevant parties in a timely manner.

4.7.2 Workers shall have access to adequate and up-to-date information about biorisk and the mitigation measures are in place to control those risks.

4.8 Other Applicable Requirements

4.8.1 The organisation shall ensure that all other relevant and applicable standards, guidelines, codes of conduct, codes of practice, legislative requirements are identified and fulfilled within the BRM system. If contents of this standard differ from applicable regulations or legislations, the facility shall satisfy the more rigorous requirements.

4.9 Preventive Actions

4.9.1 The organisation shall ensure action is taken to identify and eliminate the causes of potential non-conformities and/or to prevent their occurrence.

4.9.2 Preventive actions shall be commensurate to the effects of the potential non-conformities.

4.10 Inspection and Audit

4.10.1 The organisation shall have an inspection and audit programme so that internal inspections and audits are conducted at least once a year to determine if the BRM system conforms to the documented plans, the requirements of this standard, and if it is effectively implemented and maintained.

4.10.2 Audit findings (e.g. non-conformities and deficiencies) shall be addressed, corrective or preventive actions implemented, verified and documented.

5 RISK ASSESSMENT AND CONTROL

5.1 Risk Assessment and Control

5.1.1 Risk assessment and control are critical elements in establishing and implementing a robust BRM system. It is a systematic process to identify, assess, control, and evaluate risks.

5.1.2 The organisation shall ensure that a risk management programme is established, implemented, reviewed and maintained according to national regulations and any other applicable requirements.

5.2 Assessment Timing and Scope

5.2.1 At a minimum, risk assessment shall be carried out:

(a) prior to commencing new work or when there are significant changes to the programme of work, change management including the introduction of new personnel, hazardous biological agents and materials, or alterations to work procedures or volume;

(b) when there is new construction or modification to the facility or laboratory, plant and equipment or their operation;

(c) when there are changes to staffing arrangements, including those concerning constructors, visitors and other non-core personnel;

(d) when there are changes to SOPs or working practices (e.g. disinfectant/waste management methodologies, PPE provision, entry/exit protocols);

(e) following an incident or process failure;

(f) when there is an actual or potential non-conformity with rules and regulations (e.g. introduction of new legislation or revised legislation or regulation);

(g) when considering emergency response and contingency planning requirements; and

(h) to align with the existing management system review process (e.g. at predetermined intervals).

5.2.2 Other than operational or large-scale production/work-centric risk assessments, the facility shall undertake risk assessments for planned activities such as facility shutdown, preventive maintenance, and unforeseen incidents such as fire, major leakage of hazardous biological agents and materials, and power failure, etc.

5.3 Roles and Responsibilities

5.3.1 Risk assessment shall be conducted by a team composed of competent personnel including the biosafety manager, security manager, facility or equipment manager, scientific or technical personnel who perform the work, and any other personnel who are well versed with the procedures, hazards, and activities being assessed.

5.3.2 All risk assessments shall be reviewed and approved by the BRM committee, and these shall be appropriately documented (see Clause 4.4.4 and 4.4.5).

5.4 Hazard and Threat Identification

5.4.1 The initial step in conducting a risk assessment is to identify hazards and threats present in the facility, the processes and/or the operations. Material and pathogen safety data sheet, equipment specifications, existing SOPs (which may include work instructions, experimental protocols, and manufacturers' protocols) and facility layout shall be reviewed to identify hazards and threats, and to evaluate their associated risks. Hazards and threats can be associated with:

(a) material (e.g. hazardous biological agents and materials, non-biological hazardous materials, and their volume, concentration and environmental stability);

(b) equipment/facility (e.g. centrifuge, incubator, biosafety cabinet (BSC), bioreactor, room layout, ventilation system, potential impact associated with minor or major failure of the equipment or facility);

(c) process/activity (e.g. pipetting, plating, culturing, sampling, transferring or transporting of hazardous material);

(d) human factors (e.g. reliability, suitability and the level of competency or training); and

(e) any other factors that may affect the facility operations.

Refer to Annex C for more details on hazard and threat identification.

5.5 Risk Evaluation and Control

5.5.1 The goal of risk evaluation is to determine whether the assessed risk is acceptable or whether further targeted risk control measures should be implemented to reduce the risk.

5.5.2 Risk evaluation and control shall be conducted based on scientific knowledge, personnel experience and competency using a standardised and systematic methodology, and these shall be properly documented. Examples of methodology include Failure Mode and Effects Analysis (FMEA), Hazard and Operability Analysis (HAZOP), and Structured What-If Technique (SWIFT). Refer to MOM website (https://www.mom.gov.sg/workplace-safety-and-health/safety-and-health-management-systems/risk-management) for guidance on how to conduct an occupational safety and health risk assessment and control, and Annex F of SS 696:2023 for a biorisk-centric assessment and control.

5.5.3 A comprehensive "all-hazards approach" risk evaluation (which includes both biological and non-biological hazards) shall be undertaken. Any associated threats shall also be considered, whenever applicable. Non-biological hazards may include chemical, radiological and physical hazards (which may associate with the use of large quantity of chemicals or raw materials and heavy equipment or machinery), procedural complexity,

personnel competency and reliability, as well as resources availability and emergency scenarios. Refer to Annex C for more details on hazard and threat identification.

5.5.4 For each risk identified from the risk evaluation exercise, controls measures shall be determined. The controls may include one or more of the followings:

(a) eliminating the risk either by removing the hazard at its source or avoiding working with the hazard, and this is the most effective method of controlling risk;

(b) substituting the risk by replacing the hazard with a safer alternative such as working with a less hazardous or an attenuated biological agent, which helps to reduce the risks; and/or

(c) mitigating the risks through the use of -

(i) engineering strategies such as implementing directional airflow and physical separation of procedures, use of safety/containment equipment like BSC, isolator, bioreactor, etc.;

(ii) administrative methods such as having detailed SOPs, work instructions, training and supervision of workers; and

(iii) PPE such as protective clothing, gloves, respiratory and mucosa protection.

5.6 Implementation of Risk Control Measures

5.6.1 Plans and procedures shall be put in place to manage the implementation of the control measures identified from risk evaluation and control. This plan shall encompass the following aspects:

(a) personnel responsible and accountable for implementing the controls;

(b) resources required and ensure availability of the resources;

(c) timeline for implementation;

(d) mechanism and frequency of reviewing compliance; and

(e) process for review and approval of the plan by the BRM committee.

5.6.2 The following shall be in place before the execution of any (or new) risk control measures:

(a) SOPs are prepared or updated to include existing (or new) risk control measures and are approved by the BRM committee and management;

(b) relevant operational and maintenance procedures are developed; and

(c) the risk control measures have been communicated to the relevant personnel, with training provided whenever applicable.

5.7 Monitoring of Effectiveness

5.7.1 After the implementation of control measures, periodic reviews shall be carried out to determine if residual risk remains and is deemed acceptable. If residual risk is unacceptable and additional control measures are necessary, the management shall develop a strategy to implement further control measures to reduce the risk to an acceptable level.

5.7.2 An on-going process should also be in place to evaluate the performance of the implemented mitigation measures and the BRM system to ensure effectiveness as well as compliance with regulations and organisational requirements. A formal performance evaluation process may include planned activities such as internal audits and inspections, third-party external audits or certifications, and review by the management.

5.7.3 All information and findings from the above-mentioned exercises should be analysed and documented as evidence, and utilised to enhance the existing BRM system, as appropriate.

6 OCCUPATIONAL HEALTH PROGRAMME

6.1 Occupational Health Programme

6.1.1 The organisation shall establish an OHP that aligns with the facility's activities and risk as determined by risk assessment. The OHP shall aim to safeguard workers from illnesses resulting from exposure to hazardous biological agents or materials, or injuries sustained from activities carried out in the facility, and to support workers in the event of an exposure or accident.

6.1.2 The OHP shall incorporate a comprehensive health monitoring plan for all workers, encompassing pre-employment or pre-placement health screening (e.g. identification of significant exposure and assess their healthcare needs, including vaccination needs and PPE provision), in-employment health monitoring (e.g. regular health surveillance or screening), post-exposure management (e.g. prophylaxis treatment, medical treatment, and support), and an exit medical evaluation, whenever relevant and deemed necessary.

6.1.3 The management shall ensure that all workers are informed and made aware of their responsibility to seek medical attention and to report to occupational health professional and management if they experience illnesses or injuries attributed or suspected to be linked to the workplace. Personal medical information covered under the OHP shall be handled with strict confidentially and records are kept.

7 COMPETENCY AND TRAINING PROGRAMME

7.1 Recruitment

7.1.1 In addition to education qualifications, experience and job fit, the recruitment process should also consider reliability assessment, which includes the candidate's ability to adhere to appropriate conduct, codes of practice and aptitudes related to biorisk. Reliability assessment shall be conducted based on threat and risk assessment, and this can encompass relevant employment references, background security checks, and other appropriate measures.

7.2 Training Programme

7.2.1 A structured training programme with defined required levels of competency shall be developed based on detailed training needs assessment. The programme shall be developed by the management with advice and input from the relevant personnel and approved by the BRM committee.

7.2.2 The programme shall include initial training prior to job placement as well as refresher or continuous education. This is to ensure a consistent level of personnel competency and to enhance workers' abilities and knowledge with evolving safety and security standards of the facility.

7.2.3 The programme shall cover all personnel involved in or supporting the facility's operations, including facility workers and contractors. The programme shall cater to the

individual's respective role, responsibilities, and nature of work and aim to equip them with:

(a) a clear understanding and awareness of possible hazards, threats and risks to their health, safety and security that may arise from their work and the working environment;

(b) knowledge and skills pertaining to the concepts, tools and practices that will protect them from exposure to hazards and prevent the release of hazards to the working environment and beyond;

(c) understanding of the importance of adhering to the organisation policies, codes of conduct, codes of practice, and procedures; and

(d) awareness of potential emergency or unforeseen situations and the appropriate response actions to be taken in such circumstances.

7.2.4 Workers shall undergo assessment and demonstrate competence in BRM before they are authorised to work in the facility without supervision. Competence levels are judged on appropriate education, training and experience along with the demonstration of ability to perform their assigned responsibilities and tasks in a safe and secure manner, under conditions experienced in the workplace when performing said tasks. No personnel are exempted from demonstrating competence, irrespective of rank, experience or background.

7.2.5 Records of training and competency assessment shall be documented and filed.

7.2.6 Trainer(s) appointed to conduct training and assessing the trainees' competency shall be competent in the training areas or subjects.

7.2.7 The assessment of personnel training needs shall be reviewed every 2 years or when the worker is assigned to new duties or activities, absent from the workplace or have ceased to perform a specific task for an extended period (e.g. 6 months). Additional or refresher training shall be provided as determined by the management review process or when there are changes in the BRM programme or policy.

7.3 Human Factors and Organisational Culture

7.3.1 A positive organisational culture is important in fostering a strong sense of responsibility for safety and security among workers.

7.3.2 Management can play an important role in creating a conducive workplace environment that helps to foster and maintain a positive organisational culture. Positive organisational culture shall be established and maintained through a programme that may include but not limited to the following:

(a) human reliability and behavioural safety, including adherence to procedures;

(b) team building and motivation;

(c) communication, consultation and feedback;

(d) stress and fatigue management;

(e) conflict management and resolution;

(f) access to counselling;

(g) empowerment of all levels of personnel, including authority to correct and stop unsafe or unsecure practices;

(h) culture of willingness to report incidents or unsafe conditions/behaviours (whistleblowing), and protection of workers who do so, with the avoidance of a "blame culture";

(i) respect of individual privacy and dignity; and

(j) ergonomics, including equipment and work practices tailored to individual needs

7.4 Continuity and Succession Planning

7.4.1 Adequate backup and contingency measures should be documented and established for critical roles or individuals responsible for ensuring the safe and secure operations of the facility, in the event these individuals depart or are absent from work.

7.5 Exclusion and Reinstatement

7.5.1 Documented procedures should be in place for the prompt removal and exclusion of personnel (temporary or permanent) from the facility, where deemed necessary through risk assessment. The measures may include:

(a) remove access to the facility (e.g. taking away passes, changing locks and keys or access pass codes, and other security device); and

(b) withdraw access to information related to the facility, including documentation, computerised records and data.

7.5.2 Documented measures should be in place for re-evaluation of temporarily excluded personnel when deemed appropriate through risk assessment.

8 GOOD MICROBIOLOGICAL PRCATICES AND PROCEDURES

8.1 Good Microbiological Practices and Procedures

8.1.1 Good microbiological practices and procedures (GMPP) describe how an organisation or facility identifies and implements microbiological techniques and controls that are appropriate for the work in the organisation or facility, and these shall be documented in the BRM manual (see Clause 8.2.2)

8.1.2 All personnel who are involved in direct handling of hazardous biological agents and materials shall be competent in GMPP. More details regarding GMPP can be found in various references including the Sixth Edition of BMBL, Section 3.1 of the Fourth Edition of WHO LBM, and Section 5.11 of SS 696:2023.

8.1.3 The organisation shall ensure that allocation and provision of resources (including time, and equipment) for effective adherence of GMPP are based on appropriate risk assessment and planning, and these shall be documented.

8.2 Biorisk Management Manual

8.2.1 The organisation shall develop a facility specific BRM manual, implement and update it when necessary and make it readily available to all personnel (including workers) who may encounter hazardous biological agents and materials during their duties.

8.2.2 The manual shall contain information regarding safe and secure practices, promote a safe and secure workplace, and should cover at least the following aspects:

(a) scope and purpose of the manual;

(b) personnel roles and responsibilities;

(c) facility layout and information about emergency contact and evacuation procedures;

(d) characteristics of hazardous biological agents and materials stored or working on in the facility, and signs and symptoms of infection caused by such hazardous biological agents;

(e) comprehensive risk assessment process;

(f) good microbiological practices and procedures;

(g) special microbiological practices and procedures, if any;

(h) universal precautions, sharps policy and disposal;

(i) occupational health programme;

(j) training programme;

(k) biocontainment elements including administrative controls, specific recommended work practices, use of PPE, primary containment, facility engineering controls;

(l) biological inventory and accountability (including transfer, transport and disposal);

(m) disinfectants, decontamination and sterilisation processes and their validation;

(n) equipment maintenance and servicing;

(o) potential laboratory incidents and their responses (including immediate response, investigation, reporting and follow-up control/remediation processes);

(p) biosecurity programme;

(q) pest control programme;

(r) housekeeping programme; and

(s) facility inspection, audit or certification.

8.2.3 All personnel who may come in contact with hazardous biological agents and materials during the course of their job duties shall be deemed competent in the manual and its contents as it applies to their work.

9 PERSONAL PROTECTIVE EQUIPMENT

9.1 Personal Protective Equipment

9.1.1 Personal protective equipment needs shall be determined through a work-specific documented risk assessment, taking into consideration the specific hazardous materials that are being worked with, risks associated with the processes involved, and the availability, suitability, and ease of use of the PPE. PPE may include respirators, goggles, face shields, headcovers, laboratory coat/gown, gloves, shoes, shoe covers, hearing protection device, etc.

9.1.2 If respiratory protective equipment is used, the organisation shall establish a respiratory protection programme which includes the selection of the appropriate respirator (e.g. non-powered/tight-fitting respirator or powered air purifying respirator) with medical evaluation and fit-test to determine the appropriateness of the type of respirator (e.g. non-powered/tight-fit respirator may pose health and/or physiological burden to some wearers) and subsequent periodic fit-test, whenever applicable. Refer to Singapore

Standard Code of practice for the selection, use and maintenance of respiratory protection devices (SS 548:2022) for more details.

9.1.3 All personnel who need to use PPE are to be fitted and supplied with the correct types and sizes of PPE (e.g. respirator, gloves, shoes etc.).

9.2 Use and Maintenance of Personal Protective Equipment

9.2.1 Personnel protective equipment shall not be relied on as the primary means of protection and shall be used in conjunction with, but never as a substitute for reasonable and appropriate administrative and engineering controls.

9.2.2 Training shall be conducted to ensure all workers are proficient and compliant with the proper use, inspection, maintenance, donning and doffing of PPE, and are aware of the challenges or potential risks when using the PPE (e.g. powered air purifying respirator use can interfere downward vertical visual field, and nitrile/puncture resistant gloves can impair manual dexterity).

9.2.3 Personal protective equipment shall be utilised and maintained in accordance with established standards and manufacturer's specifications, whenever available. A schedule and associated protocols for cleaning, disinfecting, storing, inspecting, repairing, and replacement of PPE shall be in place, whenever applicable.

9.2.4 Procedures shall be in place to regularly evaluate the appropriateness and effectiveness of the PPE programme.

10 SECURITY PROGRAMME

10.1 Purpose of the Programme

10.1.1 This section addresses control measures aimed at preventing unauthorised individuals from entering the facility, accessing hazardous biological agents and materials, as well as sensitive information pertaining to, or generated by the facility.

10.2 Security Risk Assessment and Control

10.2.1 The organisation shall identify and evaluate all potential threats and vulnerabilities to determine the security needs of the facility, and these can encompass but not limited to physical, personnel, hazardous biological agents or materials, information and incident/emergency response.

10.2.2 A system shall be established to devise, implement and maintain control measures for the identified security needs.

10.2.3 Care shall be taken to coordinate biosecurity and biosafety measures to effectively manage and minimise conflicting priorities.

10.2.4 Security breaches shall be reported, recorded, and investigated. External regulatory authorities shall also be notified, if deemed appropriate.

10.2.5 A mechanism such as regular security drills shall be conducted to proactively identify vulnerabilities and monitor the effectiveness of the established control measures, and corrective actions taken to address any deficiencies identified. These shall be

documented, and lessons learnt be shared with the management and workers, whenever relevant.

10.3 Physical Security

10.3.1 Control measures shall be implemented and maintained to safeguard physical security of hazardous biological agents and materials as well as potentially contaminated materials or waste. Control measures may include:

(a) facility to be located away from uncontrolled traffic flow, and is on a secure site with perimeter control to prevent unauthorised access;

(b) facility perimeter is subject to constant monitoring (e.g. with sufficient lighting and through the use of alarms, security personnel and/or close-circuit television);

(c) measures are implemented to identify and record all personnel present in the facility, at any point in time;

(d) anti-intrusion alarms and sensors are installed, interfaces with internal and/or external security personnel or authority; and

(e) panic button or “silent” emergency alert measure is implemented (e.g. key code to alert security in the event of a hostage situation).

10.4 Personnel Reliability

10.4.1 There shall be a personnel reliability policy which outlines the process for approving and revoking access of personnel to the facility, hazardous biological agents and materials or the associated information.

10.4.2 Security awareness training shall be provided to all workers.

10.4.3 Policy and procedures shall also be applicable to external parties such as contractors, visitors, collaborators and suppliers to access the facility.

10.5 Biological Material Security

10.5.1 Hazardous biological agents and materials shall be stored in a safe and secure manner, and accessible only by authorised personnel (see Clause 10.4.1).

10.5.2 There shall be a system to maintain, control and oversee all hazardous biological agents and materials (including untreated hazardous waste) present in the facility. The oversight shall include a robust inventory management and tracking system to manage storage, acquisition, movement, usage, disposal and destruction of these biological hazardous materials (see Section 13).

10.6 Information Security

10.6.1 The organisation shall establish a policy and procedures for identifying, approving access to, and managing sensitive information. Sensitive information may include information related to hazardous biological agents and materials, technical SOPs, facility design drawing, security and maintenance plans and procedures, human resource information, etc.

10.6.2 Information can be handled securely by introducing password protected electronic records, encrypted protocols, computer with robust internet firewalls, and implementation

of good practices such as destruction of paper files and complete erasure of unwanted electronic records.

11 FACILITY PHYSICAL REQUIREMENTS

11.1 Physical Requirements

11.1.1 The physical structure of the facility shall be designed and constructed to safeguard workers, as well as other individuals and the external environment beyond the immediate work area, including other parts of the facility and the wider community from exposure to potentially hazardous biological agents and materials that may be accidentally released from the immediate work area.

11.2 Planning, Location and Design

11.2.1 The design of the facility shall be based on a formal and comprehensive assessment of the risks associated with the hazardous biological agents and materials to be used in the facility and the activities undertaken.

11.2.2 The design shall incorporate with sufficient features and services (with redundancies) to control the access, and effectively contain, manage and mitigate any possible release (of anticipated quantity) of hazardous biological agents or materials while ensuring the facility's design supports the intended activities to be carried out in the facility, i.e. large-scale production or manipulation of hazardous biological agents or materials for research, development or manufacturing purposes.

11.2.3 Design of the facility shall also comply with all local legislations, whenever applicable. Refer to Annex D for local legislations that may be applicable.

11.2.4 The following personnel shall be consulted or participated in the risk assessment and planning of the facility design:

(a) scientific or technical personnel, workers or other end users of the facility;

(b) BRM committee;

(c) biosafety manager;

(d) security manager;

(e) facility and equipment manager;

(f) designers (architects and biocontainment engineers);

(g) contractors;

(h) material and equipment suppliers;

(i) compliance personnel (personnel with knowledge in the applicable legislations and institutional requirements) or regulatory authorities; and

(j) any other relevant parties.

11.2.5 The facility shall be physically separated and isolated from main or high-traffic areas. There shall be distinct physical boundaries that separating the facility from main or high-traffic areas. Physical barriers, controlled access points, or dedicated pathways can be used to create a clear separation of the facility entrance from area accessible to the public or non-authorised personnel. Refer to Clause 10.3.1 for control measures.

11.2.6 All design features, construction techniques, materials and equipment selected shall be documented in accordance with the specified requirements.

11.2.7 New construction or physical facility modifications, including refurbishing and retrofitting, shall be in accordance with an approved plan, and be documented.

11.3 Commissioning and Decommissioning

11.3.1 There shall be a plan for commissioning and decommissioning of the facility. This plan developed at the design phase, should clearly identify all commissioning and decommissioning steps, as well as the acceptance conditions for each step as a prerequisite for proceeding to the next.

11.3.2 Commissioning shall be conducted upon the completion of facility's construction, modification or renovation; prior to the facility handover to the owner and before regulatory approval (whenever applicable); and commencement or resumption of operation. Commissioning is a process whereby a facility is subjected to a series of performance and verification tests to ensure that the facility, including equipment and containment systems therein or supported, operates in accordance with the physical design intent and specifications.

11.3.3 Decommissioning shall be performed at the end-of-life cycle of an equipment, parts of a facility or the entire facility before it is removed from service, shut down for repurposing or demolished, respectively. The decommissioning of an equipment or a facility is to ascertain that it has ceased all services or operations related to the manipulation of hazardous biological agents and materials; and is safe for disposal or shut down.

11.4 Infrastructure and Operational Management

Facility design

11.4.1 The facility, its equipment and processes shall be designed and operated in a safe and secure manner.

11.4.2 The facility shall be designed with a containment perimeter which is sealable for gaseous decontamination (fumigation). All penetrations shall be sealable to prevent uncontrolled outward airflow irrespective of the choice of primary containment equipment within. Refer to Section 12 for more details pertaining to primary containment.

11.4.3 Entry into the containment perimeter is through a double-door personnel airlock or anteroom. Features include alarms, interlocking doors or an equivalent system to ensure that only one door can be opened at any one time, and associated operating procedures are implemented to ensure the building systems function effectively all times.

11.4.4 Whenever possible, the facility should be designed to facilitate unidirectional flow of materials and personnel into/out of the containment area, with separate ways in and out.

11.4.5 Anterooms, material and personnel airlocks, must meet all requirements of spaces within the containment perimeter.

11.4.6 All containment areas where hazardous biological agents and materials are stored, handled, treated and disposed of, shall display biohazard signs. These signs shall be prominently placed at locations, rooms and equipment where the hazardous biological agents and materials are stored, handled, treated and disposed of and that only authorised personnel are permitted to enter. An emergency contact number shall be displayed at all times and kept up to date.

11.4.7 Handwashing sink and eyewash station shall be provided. Handwashing sinks are to be operated by hands-free mechanism and be provided within and near the exit of the containment perimeter.

11.4.8 The need for an emergency shower and its placement shall be determined based on a robust risk assessment. If available, measures shall be implemented to ensure that emergency shower can be carried out safely and it does not become a source of risk. Potential adverse effects arising from an emergency shower such as compatibility or reactivity between water and the hazardous chemical exposed to, ability to contain and preventing dispersion of shower water or generation of hazardous aerosol shall be considered in the risk assessment.

11.4.9 Exit from the containment perimeter shall involve specific steps and procedures that prevent exposure to contaminated PPE or personnel. Procedures for exiting the containment perimeter and the requirement for an exit (or comfort/hygiene) shower shall be determined by a facility-specific and/or a project-risk assessment.

11.4.10 All exits shall be clearly marked and emergency exit doors from the containment perimeter are equipped with alarms along with emergency by-pass mechanism.

11.4.11 When there is a pass-through equipment (e.g. pass-through box, dunk tank or autoclave) installed through containment perimeters, measures shall be in place to ensure containment is not compromised i.e. potential for cross-contamination during operation of the equipment.

11.4.12 The materials used for constructing the floors, walls, ceilings, doors, windows/viewing panels, pass-through box/equipment, and furniture shall be impermeable to liquid and chemicals, easy to clean, with smooth edges and does not chip easily to prevent cuts or injuries and able to withstand regular chemical disinfectant and fumigation.

11.4.13 Provision should be made to allow for visual monitoring of activities in the laboratory production areas where hazardous biological agents and materials are handled, either via vision panels and/or closed-circuit television cameras.

11.4.14 Windows/viewing panels at the containment barrier if any, should be fixed, sealed to the frame, airtight and shatterproof (e.g. made of tempered and laminated glass material), and all doors should be self-closing and self-latching, especially for the doors at the facility perimeter.

11.4.15 Documented procedures shall be established and executed to ensure physical components and infrastructure of the facility, and the equipment therein (see Section 12) that may have impact on biorisk are reviewed, certified, validated and maintained in a manner consistent with the BRM requirements.

Air ventilation system

11.4.16 The controlled air system shall maintain directional airflow (which provides assurance of facility biocontainment and prevention of accidental release of hazardous biological agents or materials into non-intended areas) through a dedicated ventilation system with sealable ductwork for fumigation, high-efficiency particulate arresting (HEPA) filtration of exhaust, and backdraft protection on supply. A system which includes monitors and alarms shall be in place to ensure directional airflow can be validated, on-site as well as remotely.

11.4.17 When BSC exhaust air is discharged through the building exhaust air system, the air handling system shall be designed so as not to disturb the air balance of the BSC or the room in which the cabinet is located.

11.4.18 The ventilation system shall be designed to prevent cross-contamination during fumigation.

11.4.19 Exhaust air duct serving the containment areas shall be isolated and not connected to non-containment areas, and the entire length of the exhaust ductwork (up to the exhaust fans) shall be under negative pressure during operation.

11.4.20 Air ductwork shall be constructed with material resistant to corrosion and fumigant, designed to meet stringent airtightness standards and capable to withstand the highest duct pressure that the ventilation system may generate during a system failure, as indicated by ventilation equipment technical specifications.

11.4.21 All HEPA filter units shall be designed with provision for safe decontamination, without exposing personnel and the environment from exposure to hazardous materials.

Effluent decontamination system

11.4.22 Manufacturing or large-scale production and transfer of intermediates containing hazardous biological agents and materials shall be conducted in closed systems that have been leak-tested and validated.

11.4.23 Backflow prevention mechanisms shall be installed in all liquid services/utilities passing across the containment boundary.

11.4.24 All effluent (including emergency shower water, eyewash, handwash, unsterilised autoclave condensate) from within the containment perimeter shall be decontaminated using validated procedures. Effluent and waste from facilities handling RG3 (or First Schedule BATA) biological agents or materials shall be effectively decontaminated before discharging or removing from the facility.

11.4.25 For facility handling RG3 (or BATA First Schedule) biological agents and/or RG2 biological agents which assessed to be aerosol transmissible, the room housing the effluent decontamination system (EDS) shall meet all construction, sealing and air ventilation requirements of containment space, and designed with an anteroom or airlock for controlled access. The exhaust air from the room shall also be HEPA-filtered before being discharged out. This clause may be excluded based on risk assessment, only if the following conditions are met:

(a) the biological agents (RG3 and/or RG2) and their associated materials or waste have been proven to be effectively decontaminated (i.e. rendered non-replicative and non-infectious under any conditions) before channelling or reaching the EDS in the EDS room; and

(b) adequate strategies and measures are in place to ensure that there will be no instances wherein hazardous air can be released from the EDS room into the surrounding areas or the environment.

11.4.26 The EDS room shall design to incorporate risk mitigation measures identified in the risk assessment to prevent and to respond to any spill or leak from the EDS in a safe and timely manner. The mitigation measures may include:

(a) leak-detection system;

(b) berm/pit/bund wall;

(c) sump pump; and

(d) any additional mitigations that allow for safe and timely response to EDS leaks.

11.4.27 The EDS should be sited as close to the liquid waste discharge point as possible. EDS piping shall not be enclosed but easily visualised and accessible for routine inspection.

11.4.28 The EDS shall be designed with fail-safe features that include:

(a) having the capability to hold the maximum anticipated volume of liquid waste (and the volume of disinfectant required for the decontamination process, if applicable) from the facility at any given time, or that administrative controls are implemented to prevent overflow of the waste;

(b) holding tank (if any) is designed to prevent sedimentation of waste particulates at the bottom of the tank;

(c) treatment tank is designed to ensure disinfectant homogeneity or equal heat distribution, with mechanisms to validate and monitor the effectiveness of the decontamination process;

(d) features or procedures to ensure discharge of waste content can happen only after a successfully decontamination process;

(e) an alarm system to detect and alert workers of leaks from the EDS or the connecting piping; and

(f) procedures to regularly decontaminate and clean the piping channelling the liquid waste into the EDS.

12 EQUIPMENT AND MAINTENANCE

12.1 Equipment Selection

12.1.1 The selection and utility of containment equipment shall be based on the outcome of project- and/or activity-specific risk assessments and the requirements of the activity or work. Typical containment equipment (or primary containment devices) that are used for manipulation or production of hazardous biological agents and materials include bioreactor, BSC, isolator, centrifuge and autoclave.

12.1.2 Facilities handling RG3 (or BATA First Schedule) biological agents or materials shall be equipped with a double-door pass-through autoclave, installed at the containment perimeter, with the following features:

(a) an inner door (for loading contaminated materials) opened within the containment side and an outer door (for removal of decontaminated materials) opened at the non-containment side;

(b) the two doors are interlocked;

(c) the door at the non-containment side is designed to be opened only after completion of a successful autoclave cycle;

(d) the dimension of the autoclave is correctly sized to accommodate specific laboratory equipment that need to be autoclaved;

(e) if a vacuum-assisted autoclave is used, the vacuum line is equipped with an inline HEPA filter that can be replaced without the risk of exposure;

(f) interface between the autoclave and the containment perimeter is airtight, and sealed using materials that are not easily deteriorated; and

(g) maintenance and/or servicing of the autoclave can be carried out at the non-containment side.

12.2 Equipment Performance Check

12.2.1 Performance criteria shall be defined for all critical containment equipment (e.g. primary containment devices) at the time of purchase or acquisition. The equipment shall be verified to meet the predetermined criteria through calibration, certification, commissioning and/or validation before being put in use, and thereafter to ensure continual optimal performance.

12.2.2 Performance check shall be conducted objectively by qualified or competent personnel using documented standards, tests and procedures.

Calibration, certification, commission and validation

12.2.3 Whenever applicable, containment equipment shall be calibrated and certified or commission using standards or tests to ensure its accuracy and compliance with the regulatory requirements. Calibration and certification/commissioning shall be scheduled and conducted in line with manufacturer requirements, regulatory requirements (if applicable), or at other specified intervals identified by risk assessment, whichever is earlier. For example, BSC is certified according to an appropriate standard such as National Sanitation Foundation (NSF 49), British Standard European Standard (BSEN 12469) or other equivalent standards. Refer to Section 4.9.2 of SS 696:2023 for more details regarding BSC certification.

12.2.4 For equipment that do not have relevant standards against which it can be certified/commissioned (e.g. customised containment devices), manufacturers' requirements shall be adopted. Otherwise, it shall be tested at regular intervals to ensure primary containment is maintained based on use and appropriate risk assessment of non-conformity. These must be documented.

12.2.5 All primary containment equipment shall undergo validation to ensure they meet operational requirements, before they are being used, or as per scheduled based on risk assessment.

12.3 Maintenance Programme

12.3.1 There shall be a maintenance programme covering the physical structure of the facility and equipment therein. This programme serves to ensure the safe, secure and sustainable operation of the facility and equipment. The programme also acts as pre-emptive tool to detect potential engineering and operational irregularities that may compromise containment integrity.

12.3.2 All critical features (including facility infrastructure, engineering system and equipment) shall be identified with the respective maintenance and verification procedures. The frequency of verification should be determined and established to ensure continuity to optimal functions as intended. Refer to Annex I of SS 696:2023 for examples of maintenance requirements.

12.3.3 The programme shall ensure that:

(a) sufficient redundancy capacity has been catered for critical features or equipment that support the containment of the BRM system based on risk assessment such as emergency power generator and/or uninterrupted power supply for the facility ventilation system, security system and primary containment devices; and

(b) essential spare parts (e.g. HEPA filter) are available in line with a frequency appropriate to the risk of failure and need for replacement.

12.3.4 A maintenance register shall be developed for all applicable features, engineering system and equipment.

12.3.5 All maintenance records shall be documented, updated and readily available to relevant personnel.

13 BIOLOGICAL AGENT AND BIOLOGICAL MATERIAL INVENTORY AND ACCOUNTABILITY

13.1 Inventory

13.1.1 The organisation shall be responsible for all hazardous biological agents and materials present in the facility, including the implementation of a robust inventory management and tracking system for the storage, movement, usage and destruction of such materials. Refer to Section 5.9 of SS 696:2023 for more details pertaining to biological materials inventory management and tracking system.

13.1.2 The inventory shall cover both stocks (e.g. hazardous biological agent seeds or culture isolates in the freezer/liquid nitrogen) and working materials (e.g. hazardous culture materials in the incubators or bioreactors).

13.1.3 The inventory shall be maintained as accurate, kept up to date and verifiable. The records shall be complete, well documented, retrievable, and stored securely with sufficient backup provisions.

13.2 Storage

13.2.1 All hazardous biological agents and materials shall be stored in a safe and secure location and manner, with access restricted solely to authorised personnel only.

13.3 Transfer and Transport of Biological Agents and Biological Materials

13.3.1 Movement and transportation of hazardous biological agents and materials within the facility shall be carried out safely and securely. Materials can be transported or transferred using an auto-transfer system through validated contained piping, or manually using a leak-proof and break-proof secondary container, and on a trolley if deemed necessary.

13.3.2 Transfer and transport of hazardous biological agents and materials between facilities or organisations shall be performed in accordance with organisation’s policy and national and international regulations.

13.4 Verification of Inventory

13.4.1 The inventory management system shall incorporate procedures for checking, reviewing, updating, recording and auditing. These processes are critical for ensuring accuracy,

reliability, security, tracking and effective management of hazardous biological agents and materials.

13.4.2 Internal audit on both physical and document inventory is conducted at predetermined intervals based on risk assessment. Audit results are documented, and discrepancies or findings are addressed.

13.4.3 Procedures shall be in place to detect and respond to loss, theft, diversion, or misuse of the hazardous biological agents and materials. Response may include reporting to the relevant authorities, whenever applicable.

14 WASTE MANAGEMENT, DECONTAMINATION, DISINFECTION AND STERILISATION

14.1 Waste Management and Decontamination

14.1.1 The organisation shall establish and maintain an appropriate waste management and decontamination policy, programmes and procedures.

14.2 Management of Biological Waste

14.2.1 The organisation shall establish waste management policy and implement a waste management pogramme that ensure:

(a) all hazardous, contaminated or potentially contaminated wastes (including those that may result from an emergency) have been identified along with the corresponding decontamination methodologies;

(b) all decontamination methods and procedures are validated for effectiveness and safety (refer to Annex F of SS 696:2023 for details for validation of autoclave process and performance);

(c) mixed waste (e.g. biohazardous, radioactive and/or chemical waste) is properly segregated and effectively decontaminated;

(d) waste is properly contained during storage and transport;

(e) adequate and secured space is allocated for the temporary storage of waste pending for decontamination and post decontamination pending disposal;

(f) availability of an effective waste audit trails; and

(g) compliance with regulatory requirements.

14.2.2 For facilities handling RG3 (or First Schedule BATA) biological agents and materials, all biohazardous waste generated shall be effectively decontaminated before removal (for disposal) or discharged from the facility.

14.3 Decontamination of Facility, Work Surfaces, Equipment and Laboratory Items

14.3.1 Decontamination SOPs for routine housekeeping and spill management shall be developed, documented, and implemented. The SOPs shall include the type of disinfectants and their effective working conditions. Only disinfectants that have been proven effective against the hazardous biological agent present shall be utilised, while considering compatibility issues between the disinfectants and the surfaces coming into contact.

14.3.2 All equipment and reusable items shall be thoroughly decontaminated and clearly labelled as decontaminated before they are serviced or cleaned in the laboratory, or removed from the facility for maintenance, service, repair, washing, disposal or any other purposes.

14.4 Spatial Decontamination (Fumigation of Facility)

14.4.1 The facility shall be sealable to allow for effective fumigation (e.g. in the event of a significant biological spillage and/or in the preparation of a shut-down of the facility) and prevent escape of the fumigant.

14.4.2 Procedures shall be in place to validate the efficacy of the decontamination process. Refer to Annex B of SS 696:2023 for more details on how to perform facility fumigation.

15 EMERGENCY RESPONSE AND CONTINGENCY PLAN

15.1 Emergency Response Plan

15.1.1 The organisation shall establish and maintain plans and procedures to respond to emergency scenarios that may arise from the work and operations conducted in the facility.

15.2 Emergency Scenarios

15.2.1 When planning for emergency responses, the organisation shall identify all potential and foreseeable emergency scenarios. It is unlikely that all potential scenarios are credible, but all reasonable scenarios shall be considered and recorded. Where appropriate, the rationale as to why certain scenarios or issues were dismissed should be provided.

15.2.2 Emergency scenarios that shall be considered include:

(a) infected or potentially infected worker or other contact (e.g. family member, emergency responder or community member);

(b) accident or illness of worker and the need for evacuation;

(c) spillage or release of hazardous materials, within the facility and/or to the external environment;

(d) generation or discovery of an unexpected virulent biological agent, whether from an unknown source, unidentified biological agent, or from a biological agent which was thought to be avirulent or less virulent;

(e) physical facility and equipment failure, including air ventilation system and EDS;

(f) utility failure including electricity, gas, steam, chilled water and water supplies;

(g) failure of decontamination or disinfection regime;

(h) loss of other supporting services, e.g. communication and security systems;

(i) fire or explosion;

(j) natural disaster (e.g. flood, storm, earthquake, tsunami, haze, extreme weather conditions, disease pandemics, etc.);

(k) security breach;

(l) loss of hazardous and/or security sensitive materials through theft or any other means;

(m) act of terrorism or deliberate vandalism; and

(n) intense media attention.

15.3 Emergency Response Plan and Preparedness

Plan and procedures

15.3.1 Emergency response plan shall cover all aspects, including biorisk, general safety and security, medical and environmental issues, with appropriate response and control measures proportionate to the scale and nature of the emergencies.

15.3.2 The following aspects shall be considered when developing emergency response plans and procedures:

(a) identifying the location of hazardous materials and the emergency actions required;

(b) identifying measures to control environmental impact;

(c) identifying resources including emergency responders, emergency equipment, disinfectants and consumables required and available;

(d) building on experience from previous accidents or near misses at the facility or from similar facilities; and

(e) developing plan and procedures using risk assessment, scenarios and information obtained through consultation and planning sessions with facility personnel including workers, organisational and external emergency responders.

15.3.3 The plan shall comprise:

(a) building and laboratory layouts which include emergency exit/evacuation route, assembly area, and location and nature of hazardous materials (e.g. material and pathogen safety data sheets);

(b) response procedures or SOPs for emergency scenarios and personnel evacuation;

(c) definition of roles and responsibilities of personnel involved in managing the emergencies, their assignments and contact details;

(d) listing of readily accessible resources and emergency equipment (e.g. spill kit, fire hose, fire extinguishers), their locations and maintenance status;

(e) listing of responders' PPE and communication tools, their associated maintenance programme and periodic testing of performance;

(f) listing of emergency responders (including in-house or organisation personnel, and external or national response team) and support (e.g. medical), and their contact details;

(g) listing of regulatory authorities (with contact details) to report to (depending on the type and level of emergency); and

(h) procedures for coordinating response plan processes and resources.

15.3.4 Emergency plan and procedures shall be effectively communicated to all workers and relevant parties (e.g. company emergency response team and Singapore Civil Defence Force), ensuring all are aware of their roles and responsibilities, and the response procedures.

Preparedness – training and simulation exercise

15.3.5 Regular education, training and practical drills shall be provided to responders with hands-on experience on the safe and effective use of emergency equipment.

15.3.6 Realistic and pragmatic emergency exercises or simulations shall be conducted regularly to assess and validate the emergency response plans and ascertain personnel response readiness. The exercises (including desktop and operational-based exercises or practical drills) should be realistic representations of the events that they are designed to simulate.

15.3.7 The exercises shall:

(a) be conducted under controlled conditions to ensure that they are not a source of risk in their own right;

(b) be designed to test the effectiveness of the most critical parts, and completeness of the emergency response planning process; and

(c) ensure inclusion of participation from external organisations or agencies (e.g. Singapore Civil Defence Force fire-fighting team, hazardous material team, and paramedical team), whenever possible.

15.3.8 Processes shall be in place to review the exercises, including security drills after each exercise to validate the planned responses and procedures and to identify areas for improvement.

15.3.9 All relevant lessons learnt from the exercises shall be used for improving the emergency response plans and procedures, and to be shared with all personnel including responders, workers and management.

15.4 Contingency Plan

15.4.1 The organisation shall establish contingency plans to ensure that in the event of an emergency, adequate contingency measures are in place to ensure the safety and security of on-going operations, or normal operations can be recovered quickly with minimal downtime and losses.

15.4.2 The contingency plans should:

(a) be planned during the facility design phase;

(b) identify emergencies that require contingency plan, such as from those listed in Clause 15.2.2;

(c) identify individuals who should be notified if the contingency plan is activated;

(d) identify equipment and systems that can be affected by an emergency that may cause a partial or full disruption of normal operational conditions;

(e) identify critical areas and systems for priority response and recovery of backup resources in priority order;

(f) establish a recovery time objective (minutes, hours, days, etc.) which is an acceptable time window when critical services/activities are not available. This can be varied from one service or activity to another, with some may require relocation; and

(g) put in place prevention or contingency measures such as a secure backup storage place for critical biological agents and materials (in case of a freezer breakdown),

build in sufficient redundancy and develop a partnership with other facilities that conduct similar activity or service whenever possible.

16 INCIDENT, NON-COMPLIANCE AND NON-CONFORMITY

16.1 Incident, Non-compliance and Non-conformity

16.1.1 The organisation shall establish and maintain documented procedures to define, record, report, analyse and/or learn from all non-compliances, non-conformities and incidents (accidents and near misses) related to BRM system and/or hazardous materials, containment equipment, work practices and facility infrastructure.

16.2 Incident Management Programme

16.2.1 Incident management shall include:

(a) timely response to the incident/non-compliance/non-conformity as per organisation's emergency plans and procedures. For a new incident where an existing response plan and procedures are not available, the management shall ensure that appropriate response plan and procedures are developed, if indicated by risk assessment;

(b) reporting mechanisms to internal management and relevant external (or regulatory) authorities;

(c) investigation to identify root causes of the incident/non-compliance/non-conformity; and determine if similar incident/non-compliance/non-conformity has occurred before. The investigation shall be carried out by an appropriate team composed of personnel with knowledge and skill in investigation and the subject of the investigation, and who has no known conflict of interest with the incident/non-compliance/non-conformity;

(d) identification of areas, measures, equipment or procedures that can enhance the process and prevent the occurrence or recurrence of similar incidents/non-compliances/non-conformities;

(e) reviewing and updating (as appropriate) existing risk assessments and procedures or SOPs;

(f) implementation and documentation of the changes (based on the devised preventive or corrective actions) to the BRM system; and

(g) communication of the investigation findings and follow-up actions including retraining of facility personnel or workers wherever applicable.

Annex A Designs for Anteroom (Informative)

Figure A1 illustrates the three possible designs for an anteroom.

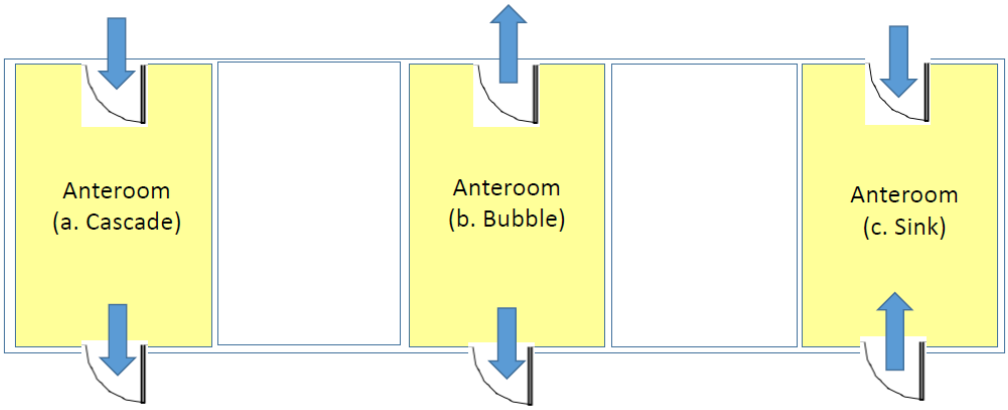

Figure A1: Examples of three possible anteroom designs with controlled airflow (a) cascade design where air flows from low to high containment area through the anteroom; (b) bubble design where air from the anteroom flows to the two adjacent areas; and (c) sink design where air from both adjacent areas flows into the anteroom. Door swing direction is for indicative purposes only.

Annex B Risk Characterisation of Biological Agent (Informative)

Table B1: Characterisation and risk classification of biological agents based on their public health and safety impact.

Country	Biological Agent Risk Level			
	Low	Moderate	High	Very high
Australian/New Zealand Standard https://ablis.business.gov.au/service/ag/australian-new-zealand-standard-as-nzs-2243-3-2010-safety-in-laboratories-microbiological-safety-and-containment/31039	RG1 (low individual and community risk) Microorganisms that are unlikely to cause human or animal disease.	RG2 (moderate individual risk, limited community risk) Microorganisms that are unlikely to be a significant risk to laboratory workers, the community, livestock, or the environment. Laboratory exposures may cause infection, but effective treatment and preventive measures are available, and the risk of spread is limited.	RG3 (high individual risk, limited to moderate community risk) Microorganisms that usually cause serious human or animal disease and may present a significant risk to laboratory workers. They could present a limited to moderate risk if spread in the community or the environment, but there are usually effective preventive measures or treatment available.	RG4 (high individual and community risk) Microorganisms that usually produce life-threatening human or animal disease, represent a significant risk to laboratory workers and may be readily transmissible from one individual to another. Effective treatment and preventive measures are not usually available.
European Union Directive 2000/54/EC https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02000L0054-20200624	Group 1 Biological agents that are unlikely to cause human disease.	Group 2 Biological agents that can cause human disease and may be hazard to workers but are unlikely to spread to the community and are usually with effective prophylaxis or treatments.	Group 3 Biological agents that can cause severe human disease and present serious hazard to workers. They may present risk of spreading to the community but are usually with effective prophylaxis or treatments.	Group 4 Biological agents that cause severe human disease and present serious hazard to workers. They may present high risk of spreading to the community and are usually no effective prophylaxis or treatments available.
Canadian Public Health Agency https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines.html	RG1 (Low individual and community risk) Microorganisms, nucleic acids, or proteins that are either (a) not capable of causing human or animal disease; or (b) capable of causing human or animal disease, but unlikely to do so.	RG2 (Moderate individual risk, low community risk) Pathogens or toxins that pose moderate risk to the health of individuals or animals, and low risk to public health and the animal population. These pathogens can cause serious disease in humans or animals but are unlikely to do so. Effective treatments and preventive measures are available and the risk of spread of disease caused by these pathogens are low.	RG3 (High individual risk, low community risk) Pathogens that pose high risk to the health of individuals or animals, and low risks to public health. These pathogens are likely to cause serious disease in humans or animals. Effective treatment and preventive measures are usually available and the risk of spread of disease caused by these pathogens is low for the public. The risk of spread to the animal population, however, can range from low to high depending on the pathogens.	RG4 (High individual risk, high community risk) Pathogens that pose high risk to the health of individuals or animals and high risk to public health. These pathogens are likely to cause serious disease in humans or animals which can often lead to death. Effective treatments and preventive measures are not usually available and the risk of spread of disease caused by these pathogens are high for the public. The risk of spread of disease to the animal population, however, can range from low to high depending on the pathogens.
United State NIH Guidelines https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf	RG1 Agents that are not associated with disease in healthy adult human.	RG2 Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available.	RG3 (High individual risk but low community risk) Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available.	RG4 (High individual risk and high community risk) Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available.

Singapore BATA* https://www.moh.gov.sg/biosafety/about-bata	Not Regulated.	Fourth Schedule Biological agents that can cause disease in humans but is unlikely to pose serious hazard, albeit some may present risk of spreading to the community. Effective treatments and preventive measures are available.	First Schedule Biological agents that usually cause serious human disease, with some may present risk of spreading to the community. Effective treatments and preventive measures are usually available.	Second Schedule Biological agents that usually cause serious or lethal human disease and may be readily transmitted from person-to-person. Effective treatments and preventive measures are not usually available.

*Note: BATA does not regulate non-pathogenic biological agents. Third Schedule biological agents refer to selected Fourth Schedule biological agents when produced in a quantity of 10 or more litres at any one time.

Annex C Potential Hazards and Threats Associated with Large-Scale Work involving Pathogenic Biological Agent or Material (Normative)

C1 Pathogenic Biological Agent

C1.1 Pathogenic biological agent can be non-genetically modified or genetically modified (GM).

C1.2 Risk assessment of biological agents is commonly based on the risk group of the parent trait of the biological agents (non-GM). Genetic modification however will add complexity to the process as modified biological agents may contain altered genetic sequences or sequences from multiple sources (biological agents which may or may not be from the same risk group) and/or exhibit altered characteristics.

C1.3 Risk assessment of GM biological agents thus, must consider the impact of genetic modification, including the risk group of the source(s) and the predicted altered functions for each of the modified sequences (addition, deletion or alteration). Unless justified otherwise, the highest risk group classification of the composite biological agents shall be adopted.

C1.3.1 For example, insertion of a virulent or toxic gene into a naive biological agent may increase the risk of the biological agent and the associated containment requirements. Inversely, certain attenuated strain or strain that has been demonstrated to have irreversibly loss of known virulence factor may qualify for a lower risk grouping, and thus, a reduction of the containment requirements compared to the risk group assigned to the parent strain.

C1.3.2 Combination of certain sequences in a new biological entity may also result in a biological agent whose risk profile is higher than that of the contributing biological agents or sequences. The synergistic function of these sequences may be one of the key attributes to consider in deciding whether a higher risk grouping and higher containment level is warranted, or until further assessments can be carried out. The initial assumption shall be that all sequences will function as they did in the original host context, unless proven otherwise.

C2 Equipment and Facility

C2.1 Mechanical functions, containment integrity and system operations of the various production equipment and utilities shall be risk assessed to ensure safety, security and performance of the entire set up.

C2.2 Containment equipment including BSC, isolator, centrifuge, bioreactor (which usually equipped with multiple penetration/connection points for sensors to monitor culture conditions, influx and efflux of raw materials and removal of byproducts) shall be critically assessed to identify if any potential weak points that can compromise the integrity of the containment.

C2.3 Hazards associated with high pressure and high temperatures generated from equipment such as bioreactor, centrifuge, autoclave, freeze dryer, vacuum pump, EDS which pose risk of explosion, and scalding or burns shall also be risk assessed critically.

C2.4 Risk-assessment shall also be extended to the facility infrastructure, with respect to the possibility of unauthorised access to the facility and the hazardous biological agents and materials therein, and accidental release of hazardous biological agents and materials.

C3 Work Process or Activity

C3.1 Risk assessment shall identify activities and procedures that may expose personnel to hazardous biological agents and materials. Many technical procedures including inoculation, propagation, sampling (for quality control), clarification, purification and concentration of culture materials, and cleaning of instrument can generate aerosol, posing risks to workers and environment.

C3.2 Risk of spillage and leakage can be a significant issue, especially if it involves large volume and/or high concentration of hazardous biological agents or materials.

C3.3 Risk of mixed use of biological agents and practices can also be an issue. Facilities that handle multiple biological agents at the same time or employ mixed practices may introduce the risk of product cross contamination and compromise biosafety if not managed properly.

C4 Human Factors

C4.1 Workers including temporary staff or outsourced staff shall be assessed on their suitability, reliability, capability and competency in performing their roles and responsibilities, job tasks assigned to them and in operating equipment in the course of their job, and their ability to respond to emergencies. Personnel health status, background checks and training can be key considerations as risk mitigation factors.

C5 Other Factors

C5.1 Risks associated with other hazards such as chemical, ergonomics and security shall also be incorporated and addressed holistically with the overall risk assessment.

C5.2 Chemical hazards may include large quantities of inactivating agents, detergents, disinfectants, caustics, adjuvants, preservatives, and solvents used in the facility.

C5.3 High energy hazards may include risk due to high voltage/current electrical energy from damaged wiring, faulty equipment, overloading, or unsafe electrical practices.

C5.4 Ergonomic hazards can be attributed to working in confined spaces, at heights, high background noise environments, and with heat-generating pressurised systems.

C5.5 Security risk associated with the possession or use of security sensitive materials, including hazardous biological agents and materials, equipment (e.g. bioreactor, freeze dryer) and information related to sensitive technologies and procedures.

Annex D Legislations (Informative)

Table D1: Examples of list of legislations that may be applicable for facilities handling hazardous biological agents and materials. The list is not exhaustive, and organisations are responsible to identify all legislations that are applicable to their facilities and the activities undertaken.

Act	Intended Purpose	Responsible Authority
Animals and Birds Act and subsidiary legislations https://www.nparks.gov.sg/avs/resources/legislation/animals-and-birds-act-chapter-7	An Act for preventing the introduction into, and the spreading within, Singapore of diseases of animals, birds or fish; for the control of the movement of animals, birds or fish into, within and from Singapore; for the prevention of cruelty to animals, birds or fish; for measures pertaining to the general welfare and improvement of animals, birds or fish in Singapore and for purposes incidental thereto.	National Parks Board
Biological Agents and Toxins Act and subsidiary legislations https://www.moh.gov.sg/biosafety/about-bata	An Act that regulates the import, transhipment, possession, use (including large-scale production), transfer and transportation of biological agents and toxins. It is intended to ensure that biological agents and toxins are used safely and responsibly to prevent any harm to public health, safety, and the environment.	Ministry of Health
Environmental Protection and Management Act and subsidiary legislations https://www.nea.gov.sg/corporate-functions/resources/legislation-international-law/legislation	An Act to consolidate the laws relating to environmental pollution control, to provide for the protection and management of the environment and resource conservation, and for purposes connected therewith.	National Environmental Agency
Fire Safety Act and subsidiary legislations https://www.scdf.gov.sg/home/fire-safety/downloads/acts-codes-regulations	An Act to make provisions for fire safety and for matters connected therewith.	Singapore Civil Defence Force
Health Products Act and subsidiary legislations https://www.hsa.gov.sg/therapeutic-products/overview	An Act to regulate the manufacture, import, supply, presentation and advertisement of health products and of active ingredients used in the manufacture of health products and provide for matters connected therewith.	Health Sciences Authority
Infrastructure Protective Act and subsidiary legislations https://www.police.gov.sg/Advisories/Infrastructure-Protection/Infrastructure-Protection-Act	An Act to provide for the protection of certain areas, places and other premises in Singapore against security risks.	Ministry of Home Affairs
Public Utilities Act and subsidiary legislations https://www.pub.gov.sg/Pages/LegislationandRequirements.aspx	An Act to reconstitute the Public Utilities Board and for matters connected therewith.	Public Utilities Board

Sewage and Drainage Act and subsidiary legislation https://www.pub.gov.sg/Pages/LegislationandRequirements.aspx	An Act to provide for and regulate the construction, maintenance, improvement, operation and use of sewerage and land drainage systems, to regulate the discharge of sewage and trade effluent and for matters connected therewith.	Public Utilities Board
Strategic Goods (Control) Act and subsidiary legislation https://www.customs.gov.sg/businesses/strategic-goods-control-1/overview/legislation/	An Act to control the transfer and brokering of strategic goods, strategic goods technology, goods and technology capable of being used to develop, produce, operate, stockpile or acquire weapons capable of causing mass destruction, and missiles capable of delivering such weapons; and for purposes connected therewith.	Singapore Customs
Workplace Safety and Health Act and subsidiary legislation https://www.mom.gov.sg/workplace-safety-and-health/workplace-safety-and-health-act	An Act relating to the safety, health and welfare of persons at work in workplaces.	Ministry of Manpower

REFERENCES

1 Australian/New Zealand Standard, Sixth Edition (2020). Standards Australia Limited/Standards New Zealand.

2 Biological Agents and Toxins Act 2005 (2024). Singapore Statutes Online.

3 Biosafety in Microbiological and Biomedical Laboratories, Sixth Edition (2020). U.S. Department of Health and Human Services Public Health Service, Centers for Disease Control and Prevention National Institutes of Health.

4 BSEN 12469 (2000). Biotechnology. Performance Criteria for Microbiological Cabinets.

5 Canadian Biosafety Standard, Third Edition (2022). Government of Canada.

6 EN 1822 (2019). European Standard for Filters.

7 Global Action Plan for Poliovirus Containment, Fourth Edition (2022). World Health Organization.

8 ISO 29463-5 (2022). High-efficiency Filters and Filter Media for Removing Particles in Air.

9 Laboratory Biosafety Manual, Fourth Edition (2020). World Health Organization.

10 NIH Guideline for Research involving Recombinant or Synthetic Nucleic Acid Molecules (2019). Department of Health and Human Services, National Institute of Health.

11 NSF/ANSI 49 (2022). Biosafety Cabinets Design and Performance.

12 Pedrosa PBS and Cardoso TAO (2011). Viral infections in workers in hospital and research laboratory settings: a comparative review of infections modes and respective biosafety aspects. International Journal of Infectious Diseases. 15: e336-e376.

13 Singapore Standard (SS) ISO 35001:2021 Biorisk management for laboratories and other related organisations. Enterprise Singapore.

14 Singapore Standard (SS) 548:2022 Code of practice for the selection, use and maintenance of respiratory protection devices. Enterprise Singapore.

15 Singapore Standard (SS) 696:2023 Specification for high containment (biosafety level 3) facility. Enterprise Singapore.

ACKNOWLEDGEMENTS

This guideline is developed by a workgroup with the following personnel. Members of the Expert Panel and Reviewers were contributed within their individual capacity.

	Expert Panel	**Affiliation**
Chair	Assoc Prof Raymond Lin	*National Public Health Laboratory*
Members	Mr Dan Yoong	*World BioHazTec (Singapore)*
	Mr David Lam	*Singapore General Hospital*
	Dr Sabai Phyu	*Laboratory Biorisk Consultancy & Training*
	Dr Tessy Joseph	*National University of Singapore*
	Expert Reviewer	
Biorisk	Dr Paul Huntly	*Riskren Pte Ltd*
GMP	Dr Kang Teng Ong	*Health Sciences Authority*
	Secretariat	
	Mr Chern Chiang Siew	*National Public Health Laboratory*
	Dr Su Yun Se Thoe	*Ministry of Health*