भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
जैव प्रौद्योगिकी विभाग
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

सत्यमेव जयते

आज़ादी का अमृत महोत्सव

ब्लॉक-2, (6-8वाँ तल), एवं ब्लॉक-3, (4-5वाँ तल)
सी0जी0ओ0 कॉम्प्लेक्स लोधी रोड, नई दिल्ली-110003
Block-2 (6-8th Floor) and Block-3 (4-5th Floor)
C.G.O. Complex, Lodhi Road, New Delhi-110003
Tele : 011-24365071 Fax : 011-24362884
Website : http://www.dbtindia.nic.in

No. PID-15011(11)/5/2020-PPB-DBT **Dated 27.09.2024**

OFFICE MEMORANDUM

Sub.: National Guidelines for the Establishment and Certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024

In India, all activities related to Genetically Engineered organisms (GE organisms) or cells and hazardous microorganisms and products thereof are regulated as per the "**Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989**" (Rules, 1989) notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India under the Environment (Protection) Act, 1986 (EPA 1986).

2. Department of Biotechnology notified the "**Guidelines for the Establishment of Containment Facilities: Biosafety Level 2 (BSL-2) & 3 (BSL-3) and Certification of BSL-3 facility, 2020**", detailing the important considerations for establishing the BSL-3 facilities, technical standards for engineering controls, essential tests to be conducted during the installation, validation procedures, Standard Operating Procedures and Certification mechanism. Further, "**General Guidelines for Establishment of Biosafety Level-3 Laboratories, 2019**" notified by ICMR provides comprehensive information on objectives and scope of BSL-3 laboratory facilities, specific laboratory designs, construction considerations, staffing and pertinent issues related to the operation and maintenance of these facilities.

3. In order to ensure uniform technical specifications for the establishment and certification of BSL-3 facilities, it was deemed necessary by the Department of Biotechnology and Indian Council of Medical Research, to issue a collaborative guidance document, to outline the design, facilities and procedures for establishment and certification of a BSL-3 facility.

4. In view of the above, "National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility" was drafted by the Working group, constituted by ICMR for the purpose, under the Chairmanship of Dr. Manmohan Parida (Director, DRDE Gwalior).

5. The Department of Biotechnology hereby notifies the "**National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024**". The guideline supersedes the "Guidelines for the Establishment of Containment Facilities: Biosafety Level 2 (BSL-2) & 3 (BSL-3) and Certification of BSL-3 facility, 2020".

6. The Guidelines can be accessed from **https://ibkp.dbtindia.gov.in/**.

7. It is important to note that specifications for BSL-3 facility are essential components of compliance required for the Certification of the facility.

8. With this notification, Certification of BSL-3 laboratories shall be binding Pan-India for all public and private organizations engaged in handling of GE organisms and hazardous microorganisms requiring BSL-3 facility, for Research and Development purpose w.e.f. 27.09.2024.

9. The Certification of BSL-3 facility of Central Government entities shall be dealt by the concerned Line Ministry of the Government of India. The Certification of BSL-3 facility of State Government entities pertaining to the Ministry of Health shall be dealt by DHR, ICMR/DoH&FW, while other State Government institutions shall be dealt by DBT. In respect of all other entities, i.e., Non-Governmental Organizations, Certification shall be dealt by DBT.

10. The Guidelines have approval of the Review Committee on Genetic Manipulation (RCGM), a Competent Authority notified under the Rules, 1989 of the Environment (Protection) Act, 1986; which approved the guidelines in its 290th meeting held on 07.08.2024.

(Dr. Nitin Kumar Jain)
Member Secretary, RCGM &
Scientist- 'G', Department of Biotechnology

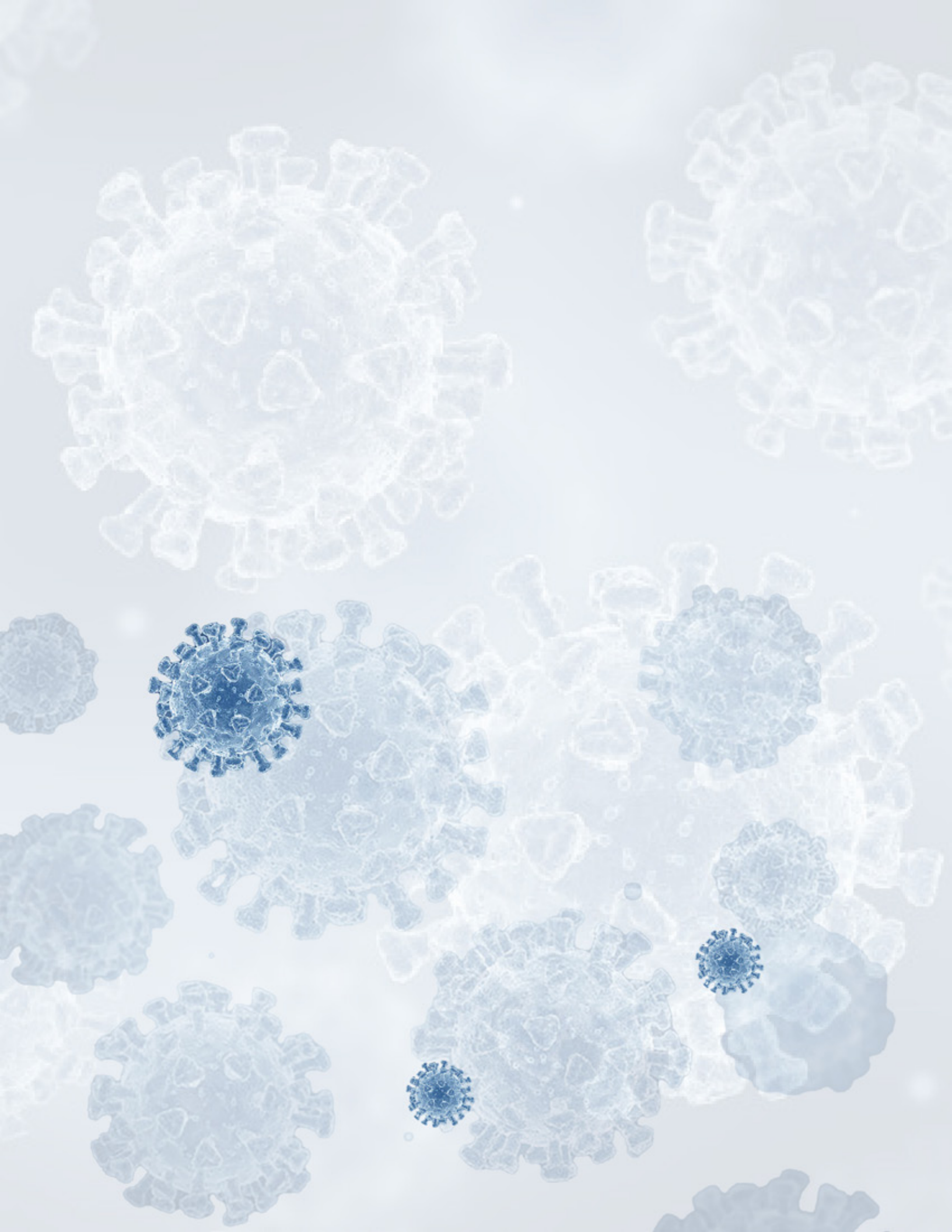
Department of Biotechnology
Ministry of Science & Technology
Government of India

Department of Health Research
Ministry of Health and family Welfare
Government of India

ICMR
INDIAN COUNCIL OF MEDICAL RESEARCH

NATIONAL GUIDELINES FOR THE ESTABLISHMENT AND CERTIFICATION OF BIOSAFETY LEVEL-3 (BSL-3) CONTAINMENT FACILITY

2024



सत्यमेव जयते

डॉ. राजेश सु. गोखले
Dr. RAJESH S. GOKHALE

आज़ादी का अमृत महोत्सव

सचिव
भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
जैव प्रौद्योगिकी विभाग
ब्लॉक-2, 7वां तल, सी.जी.ओ कॉम्पलेक्स
लोधी रोड़, नई दिल्ली-110003

SECRETARY
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY
Block-2, 7th Floor, CGO Complex
Lodhi Road, New Delhi-110003

Message

The establishment of Biosafety Level-3 (BSL-3) containment facilities is a critical component in ensuring the safe handling of pathogens that pose serious or potentially lethal risks to public health and safety. These laboratories are designed to manage and mitigate the hazards associated with infectious agents that may spread through aerosol transmission, making them essential for both research and diagnostic purposes.

In this regard, the Department of Biotechnology is delighted to release the "**National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024**". These guidelines have been prepared though extensive deliberations of the 'Working Group' constituted by the Indian Council of Medical Research (ICMR), for the purpose and the Review Committee on Genetic Manipulation (RCGM) constituted under the Department of Biotechnology, Ministry of Science and Technology. I appreciate the efforts of all the officers and experts of the 'Working Group' and RCGM for drafting the guidance document on establishment and certification of BSL-3 facilities.

This document provides comprehensive guidelines to assist in the establishment, operation, and certification of BSL-3 facilities across the nation. It serves as a resource for institutions and professionals involved in the construction, operation, and regulation of these high-containment laboratories.

The guidelines herein address all key aspects of BSL-3 facility operations, including the design of containment systems, engineering controls, safety protocols, and personnel training. Additionally, the guidelines emphasize the importance of strict adherence to international biosafety standards and best practices, which are crucial for ensuring the safety of personnel, the surrounding community, and the environment.

We encourage all stakeholders to familiarize themselves with these guidelines and integrate them into the design and management of their facilities. By adhering to these standards, we collectively strengthen our national capacity to handle and respond to high-risk pathogens, safeguard public health, and foster innovation in biomedical research.

Thank you for your commitment to safety and excellence in biosafety practices.

(Dr. Rajesh S. Gokhale)

Phone : 24362950/24362881, Fax : 011-24360747, E-mail : secy.dbt@nic.in

सत्यमेव जयते
डॉ. राजीव बहल, एमडी, पीएचडी
DR. RAJIV BAHL MD, PhD

सचिव, भारत सरकार
स्वास्थ्य अनुसंधान विभाग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय एवं
महानिदेशक
भारतीय आयुर्विज्ञान अनुसंधान परिषद
Secretary, Government of India
Department of Health Research
Ministry of Health & Family Welfare
Director-General
Indian Council of Medical Research

Foreword

The containment biosafety facilities, such as Biosafety Level-3 (BSL-3) laboratories, are critical components in the global infrastructure for managing and mitigating biological risks. The presence and proper functioning of high containment biosafety facilities are indispensable for safeguarding public health, advancing scientific knowledge, and enhancing global health security. BSL-3 facilities are integral to the safe handling of high-risk pathogens, providing a controlled environment that protects laboratory personnel, the public, and the environment from potential biological hazards. Planning and establishment of the BSL-3 facility must be built on some national or international standards to have robust and reliable containment system. The stringent containment measures, such as construction and engineering controls in BSL-3 facilities are the backbone of biosafety, providing the necessary physical and operational barriers to contain high-risk pathogens. These controls are essential for protecting laboratory personnel from exposure, preventing the escape of pathogens into the public domain, and safeguarding the environment from contamination.

To provide detailed guidance on the essential requirements for the establishment, operation, and certification of BSL-3 facilities, which are crucial for handling high-risk pathogens and genetically engineered organisms, the "**National Guidelines for the Establishment and Certification of Biosafety Level-3 (BSL-3) Containment Facility**" are issued in collaboration between the Department of Biotechnology (DBT), Ministry of Science & Technology, and the Indian Council of Medical Research (ICMR), Department of Health Research (DHR), Ministry of Health & Family Welfare. These guidelines aim to ensure uniform technical specifications and standardized practices across all BSL-3 facilities in India, thereby enhancing biosafety and biosecurity measures nationwide. This document describes the design, facilities, procedures, and certification mechanism for BSL-3 facilities.

The document provides comprehensive national guidelines for establishing and certifying Biosafety Level-3 (BSL-3) containment facilities in India. Compliance with these guidelines fosters global standards, enhancing the ability to respond to biological threats and advancing scientific research safely.

It is strongly recommended to follow these guidelines across India for all BSL-3 containment facilities in public and private organizations involved in handling genetically engineered (GE) organisms and high-risk pathogens for Research & Development, diagnostics, and other support services.

Rajiv Bahl

(**Rajiv Bahl**)

V. Ramalingaswamy Bhawan, Ansari Nagar, New Delhi - 110 029
Tel.: 011-26588204, Website : www.icmr.gov.in, E-mail : secy-dg@icmr.gov.in

सत्यमेव जयते

स्वच्छ भारत
एक कदम स्वच्छता की ओर

भारत सरकार
विज्ञान और प्रौद्योगिकी मंत्रालय
बायोटेक्नोलॉजी विभाग
ब्लाक 2, 7वां तल, सी0 जी0 ओ0 कम्पलेक्स
GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY
Block-2, 7th Floor C.G.O. Complex
Lodhi Road, New Delhi-110003

PREFACE

In exercise of powers conferred through Environment (Protection) Act, 1986 and "**Rules for the manufacture, use/import/export and storage of hazardous microorganisms/ genetically engineered organisms or cells, 1989**" (Rules, 1989), the Review Committee on Genetic Manipulation (RCGM), Department of Biotechnology (DBT), Government of India, notified the "**Guidelines for the Establishment of Containment Facilities: Biosafety Level 2 (BSL-2) & 3 (BSL-3) and Certification of BSL-3 facility, 2020**", detailing the important considerations for establishing the BSL-3 facilities, technical standards for engineering controls, essential tests to be conducted during the installation, validation procedures, Standard Operating Procedures and Certification mechanism. Further, "**General Guidelines for Establishment of Biosafety Level-3 Laboratories, 2019**" notified by ICMR provides comprehensive information on objectives and scope of BSL-3 laboratory facilities, specific laboratory designs, construction considerations, staffing and pertinent issues related to the operation and maintenance of these facilities.

In order to ensure uniform technical specifications for the establishment and certification of BSL-3 facilities, it was deemed necessary by the Department of Biotechnology and Indian Council of Medical Research, to develop a collaborative guidance document, outlining the design, facilities and procedures for establishment of a Biosafety Level-3 (BSL-3) facility and its certification mechanism.

We acknowledge the critical inputs provided by the esteemed Experts of the Working group and RCGM to prepare these comprehensive Guidelines. We also acknowledge contribution of Biosafety Support Unit (BSU), Regional Centre for Biotechnology, in preparation of this guidance document.

We are glad to present the "**National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024**", which supersedes the "Guidelines for the Establishment of Containment Facilities: Biosafety Level 2 (BSL-2) & 3 (BSL-3) and Certification of BSL-3 facility, 2020". The purpose of this Guidelines is to provide guidance on Pre-requisites for the construction, Pre-design considerations, Construction of the laboratory, Technical standards for engineering controls, Essential tests during Commissioning, Validation procedure, Standard Operating Procedures (SOPs) for specific considerations for working and Certification mechanism, to Stakeholders including the Architect, Engineer, Contractor, Management, Facility Incharge and Regulators, for establishment and Certification of a BSL-3 facility.

Herein, the Certification of BSL-3 facility of Central Government entities shall be dealt by the concerned Line Ministry of the Government of India, while that of State Government entities pertaining to the Ministry of Health shall be dealt by DHR, ICMR/DoH&FW, while other State Government institutions shall be dealt by DBT. In respect of all other entities, i.e., Non-Governmental Organizations, Certification shall be dealt by DBT. This is to ensure the effectiveness and strengthening of the Certification mechanism of BSL-3 facility and address laboratory biosafety and biosecurity practices.

These guidelines shall be applicable Pan-India to all BSL-3 containment facilities, available in both public and private organizations, involved in handling of high-risk group microorganisms and GE organisms, for research and development purpose.

Prof. Y. K. Gupta
Chairman, RCGM
Former Director IITR, Lucknow
& President, AIIMS, Jammu

Dr. Nitin K Jain,
Scientist G, DBT & Member Secretary, RCGM

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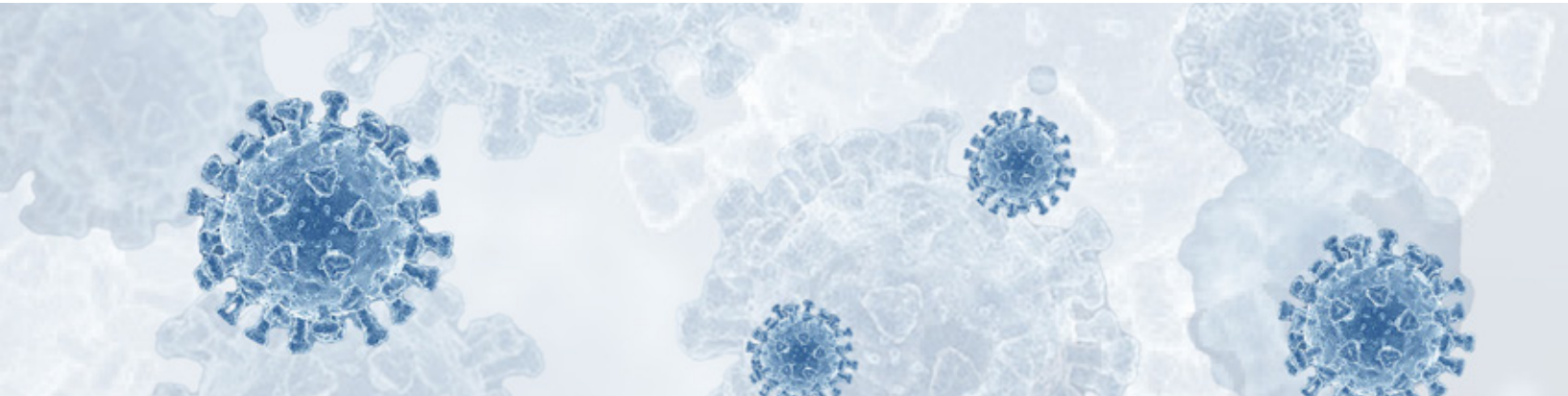
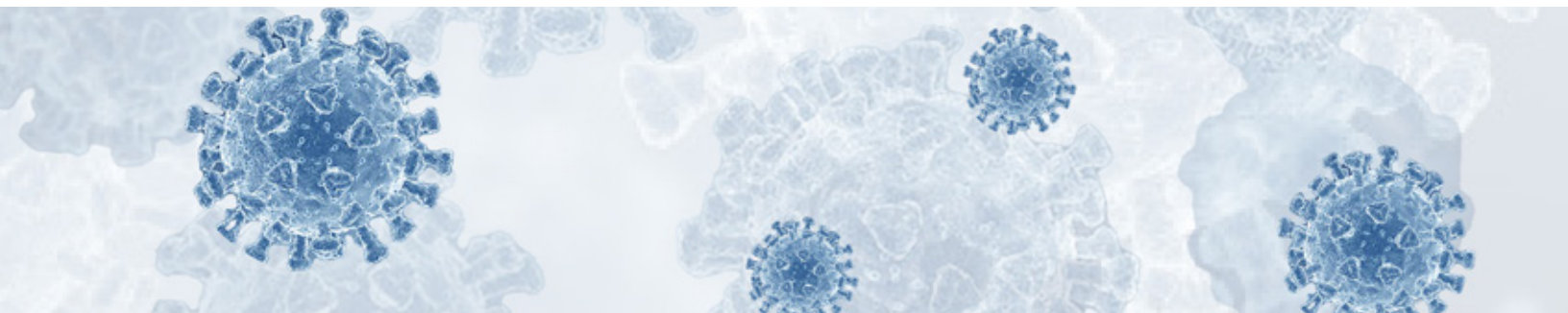
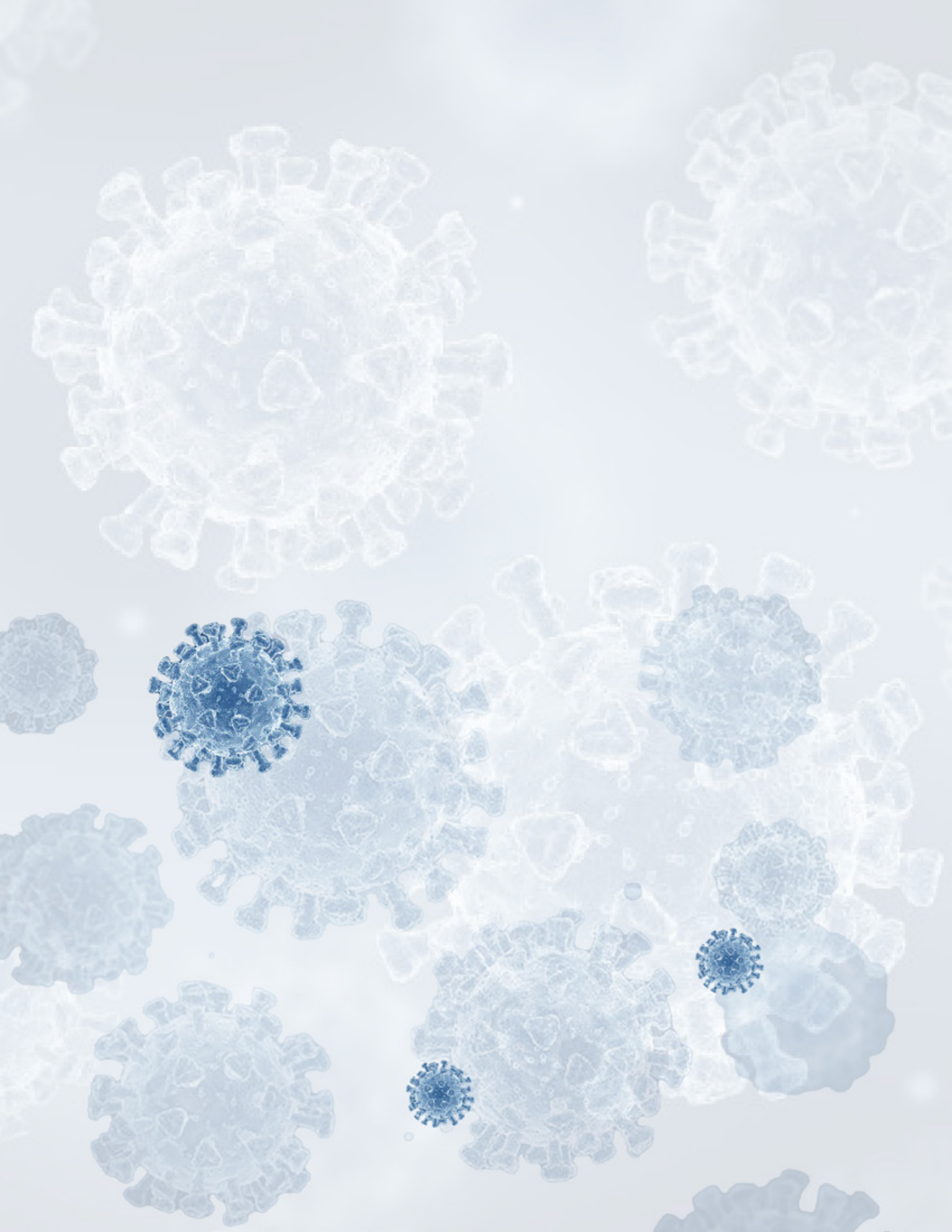


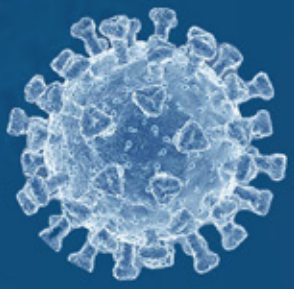
ABBREVIATIONS

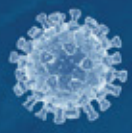
ACPH	Air Changes Per Hour
ACR	Air Change Rate
AMC	Annual Maintenance Contract
BAS	Building Automation System
BC	Biological Containment
BIBO	Bag-In-Bag-Out
BMS	Building Management System
BSC	Biosafety Cabinet
BSL	Biosafety Level
CCTV	Closed-Circuit Television
CDC	Centers for Disease Control and Prevention
CPCB	Central Pollution Control Board
DBT	Department of Biotechnology
DDC	Direct Digital Control
DG	Diesel Generator
DST	Department of Science and Technology
ECBC	Energy Conservation Building Code
EPA	Environment (Protection) Act
ETP	Effluent Treatment Plant
GE	Genetically Engineered
GEAC	Genetic Engineering Appraisal Committee
HEPA	High-Efficiency Particulate Air
HVAC	Heating, Ventilation and Air Conditioning
IATA	International Air Transport Association
IBSC	Institutional Biosafety Committee
ICAR	Indian Council of Agricultural Research
ICMR	Indian Council of Medical Research
IEC	International Electrotechnical Commission
ISO	International Organization for Standardization
ISO/IEC 15189	Accreditation based on standards entitled “General requirements for the competence of medical laboratories”, published by the International

	Organization for Standardization
ISO/IEC 17025	Accreditation based on standards entitled “General requirements for the competence of testing and calibration laboratories”, published by the International Organization for Standardization
ISO 20387	Accreditation based on standards entitled “Biotechnology - Biobanking - General requirements for biobanking”, published by the International Organization for Standardization.
LAN	Local Area Network
MoEF&CC	Ministry of Environment, Forest and Climate Change
NSF/ANSI 49	American National Standard, which apply to Class II Biosafety Cabinets
PERT	Project (or Program) Evaluation and Review Technique
PLC	Programmable Logic Controller
PPE	Personal Protective Equipment
QA	Quality Assurance
RCGM	Review Committee on Genetic Manipulation
rDNA	Recombinant DNA
RG	Risk Group
SOPs	Standard Operating Procedures
SS-304	Stainless Steel - Grade 304 (Standard “18/8”)
ULPA	Ultra-Low Particulate Air
UPS	Uninterrupted Power Supply
VAV	Variable Air Volume
VFD	Variable Frequency Drive
WHO	World Health Organization

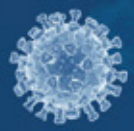








INTRODUCTION



INTRODUCTION

In the past, India has witnessed several outbreaks of emerging / re-emerging infections such as Vibrio cholerae O139 (1997 to 2006 and 2009 to 2017), Nipah virus (2001, 2007 and 2018); SARS-CoV (2003); Avian Influenza H5N1 (2006); ECSA strain of Chikungunya virus (2006); pandemic Influenza (2009); Ebola virus (2014), Zika virus (2016, 2019 and 2024), SARS-CoV-2 (2020) and Avian influenza A (H5N8) in 2021. The country also faces threats of infiltration of new or exotic viruses such as Yellow fever virus and Middle East Respiratory Syndrome-coronavirus (MERS-CoV). Such infectious agents are referred to as high-risk pathogens as these have potential to cause serious fatal disease and might also result in pandemics. Simultaneously, the rapid advances and innovations in the field of Biotechnology over the last few decades for the development of diagnostics, prophylactics and therapeutics, have led to application of genetic manipulation and generation of Genetically Engineered (GE) organisms, requiring the addressal of biosafety risks. Diagnostic or research work on the high-risk pathogens or GE organisms must be conducted by properly trained personnel in a laboratory equipped with appropriate design features, containment practices, engineering controls and standard operating procedures, as mentioned in the current guidelines; to minimize the risk to both working personnel and community-at-large. Such a facility is referred to as a containment laboratory or Biosafety level 3 (BSL-3) laboratory.

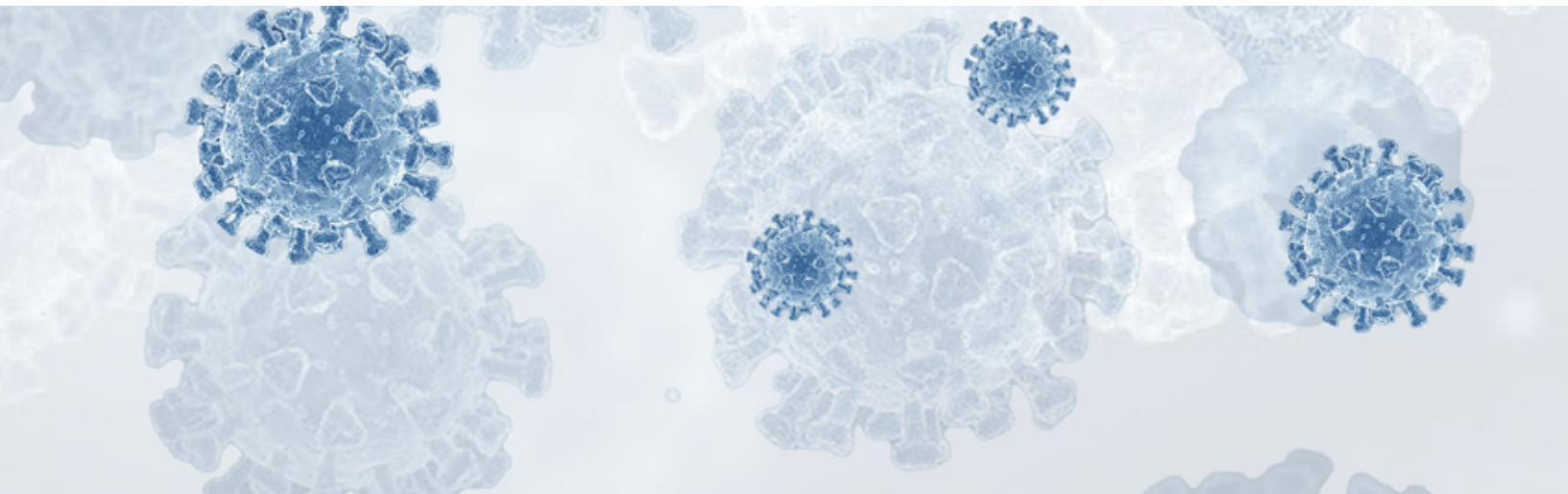
To strengthen the country's capacity to respond to outbreaks, to support diagnosis of unknown pathogens and to facilitate research and development work on high-risk pathogens and GE organisms, the Government of India has established several BSL-3 laboratories in public sector R&D as well as academic institutions. Besides these, private sector including the industries and private universities has also established such facilities to facilitate research and development. For ensuring the protection of research personnel, health of public in general and the environment, it is mandatory that such facilities are built as per harmonized regulations and guidelines and the work practices in such facility follow a standard code-of-conduct.

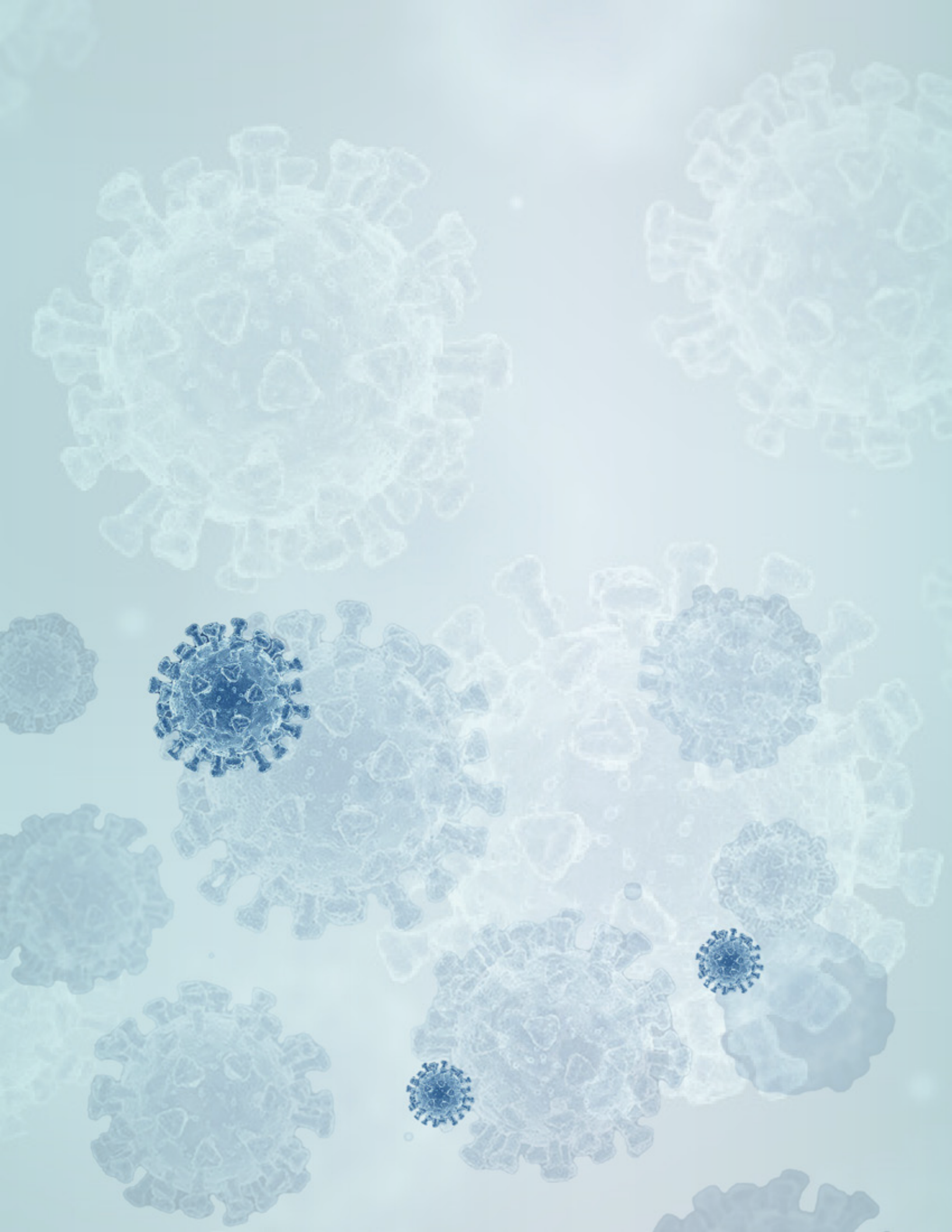
In India, all activities related to Genetically Engineered (GE) organisms or cells and hazardous microorganisms (HMO) and products thereof are regulated as per the *"Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989" (Rules, 1989)* notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India under the Environment (Protection) Act, 1986 (EPA 1986). The Review Committee on Genetic Manipulation (RCGM), one of the competent authorities as per the provisions of Rules, 1989 functions in the Department of Biotechnology to monitor the safety-related aspects in respect of on-going research projects and activities involving hazardous microorganisms, genetically engineered organisms and cells and products thereof; and to issues guidelines specifying procedure for regulatory processes with respect to activities involving genetically engineered organisms in research, use and applications including industry with a view to ensure environmental safety. All ongoing projects involving high-risk category and controlled field experiments are reviewed by RCGM to ensure that adequate precautions and containment conditions are followed as per the guidelines. RCGM also provides regulatory oversight for all such activities.

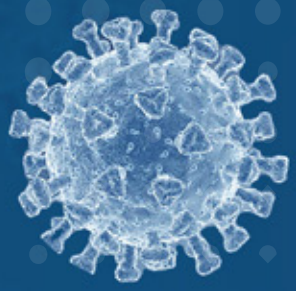
These containment facilities should have specific engineering features and follow standard containment practices to prevent threats to health security and environment. Given the handling of high-risk pathogens and high consequence research and development work being undertaken in such facilities, it is crucial to institute a certification mechanism to ensure that the facilities meet the requirements for essential design features, containment practices, and engineering controls. Furthermore, Standard Operating Procedures (SOPs) for specific considerations to work in the BSL-3 facility must be developed and implemented, to minimize the risks associated with laboratory operations and ensure the protection of the laboratory worker(s) and the environment. Certification of such facilities should be ensured before initiation of research work and essential parameters should be validated annually or after any program change or replacement of critical heating, ventilation and air conditioning (HVAC)/exhaust system components that may affect the laboratory's operating environment. This is essential for the research integrity as well as the safety of people and the environment.

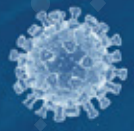
In this regard, ICMR and DBT have notified guidelines for establishment and certification of BSL-3 labs. *"General Guidelines for Establishment of Biosafety Level-3 Laboratories, 2019"* notified by ICMR provide comprehensive information on objectives and scope of BSL-3 laboratory facilities, specific laboratory designs, construction considerations, staffing and pertinent issues related to operation and maintenance of these facilities. The *"Guidelines for the Establishment of Containment Facilities: Biosafety Level 2 (BSL-2) & 3 (BSL-3) and Certification of BSL-3 facility, 2020"* notified by DBT, details the important considerations for establishing the BSL-3 facilities, technical standards for engineering controls, essential tests to be conducted during the installation, validation procedures, Standard Operating Procedures and Certification mechanism.

In order to ensure uniform technical specifications for the establishment and certification of BSL-3 facilities, it was deemed necessary for the Department of Biotechnology and Indian Council of Medical Research, to issue a collaborative guidance document. This document will outline the design, facilities and procedures for establishment of a Biosafety Level-3 (BSL-3) facility and its certification mechanism. These guidelines shall be binding Pan India to all BSL-3 containment facilities, available in both public and private organizations, involved in handling of GE organisms and high-risk group pathogens for research and development purpose. DBT nominees of the Institutional Biosafety Committees (IBSCs) must ensure that the work involving GE organisms and high-risk group pathogens (RG-3 and above) should be initiated only after the certification of BSL-3 facilities according to the laid-out guidelines and approval of the research project by IBSC and RCGM.



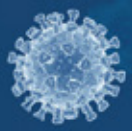






CHAPTER 1

BIOSAFETY PROGRAMME MANAGEMENT



CHAPTER 1: BIOSAFETY PROGRAMME MANAGEMENT

In India, all activities related to GE organisms or cells and hazardous microorganisms and products thereof are regulated as per the *"Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989" (Rules, 1989)* notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India under the Environment (Protection) Act, 1986 (EPA 1986).

As per the Rules, 1989, Review Committee on Genetic Manipulation (RCGM) functions in the Department of Biotechnology to monitor the safety related aspects in respect of on-going research projects and activities involving genetically engineered organisms/ hazardous microorganisms. RCGM brings out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving genetically engineered organisms in research use and applications including industry with a view to ensure environmental safety. All ongoing projects involving high-risk category and controlled field experiments are reviewed to ensure that adequate precautions and containment conditions are followed as per the guidelines.

The Institutional Biosafety Committee (IBSC) needs to be constituted by an organization, including research institutions, or any person handling hazardous microorganisms/ genetically engineered organisms. IBSC is solely responsible to implement and respond to institutional biosafety and biosecurity, and evaluation of applications/ reports related to rDNA technology work involving the GE organisms and non-GE hazardous microorganisms in an organization. IBSC functions as the nodal point for the implementation of the biosafety guidelines and the interactions within the institution.

The effective management of biological risks is supported by biosafety measures established at National and Institutional levels. RCGM provides regulatory framework for assessing and managing biological risks, and implementing a structured biosafety oversight system. Further, the IBSCs have been authorized to assess the biological risks in their program and facilities and ensure appropriate risk control measures to protect their personnel, community and the environment. This process requires an organization to develop a biosafety program: a set of tools, information and associated actions that are monitored and continuously evolved based on national regulations and international guidance. The Biosafety regulatory framework in India provides measures for:

- Mechanisms to appropriately address and manage the risks associated with GE organisms or cells and non-GE hazardous microorganisms and products thereof have been provided.
- Practice and procedure to manage risk inherent to GE organisms or cells and non-GE HMOs are in place.
- Manuals of guidelines specifying a procedure for regulatory process with respect to activities involving GE organisms or cells and non-GE HMOs ensuring human health and environmental safety are prepared, periodically updated/ revised and implemented.

- The protocols for generating biosafety data to address the challenges raised by the emerging new areas of Biotechnology such as Genome Editing, Cell therapy are being developed.
- A framework has been developed for the functioning and coordination of competent authorities.
- The roles and responsibilities of competent authorities and their respective members have been defined.
- Appropriate training of personnel in biosafety awareness and practices is regularly conducted.
- Activities related to laboratory biosafety and its associated policies and procedures, are aligned with national and international guidelines and regulations.
- A framework has been developed for ensuring laboratory biosecurity practices.
- Provides a communication platform for the scientific community and other stakeholders through Indian Biosafety Knowledge Portal (IBKP) and Biological Research Regulatory Approval Portal (BioRRAP).

This chapter provides an overview of the foundational elements of biosafety, which provide a framework for the most effective biosafety program at the Institutional and National level.

1.1 Biosafety Culture and Policy

Managing biological risks requires an organizational culture that ensures the biosafety and biocontainment of risk-inherent microorganisms, infectious disease agents and toxins, in addition to responsibly conducting research and development activities, complying with relevant laws, regulations, guidelines, and policies, as well as emphasizing on the Biosafety culture. Biosafety culture refers to the set of norms, values, beliefs and patterns of behaviour instilled and facilitated in an environment by individuals working together to support or enhance best practices for laboratory biosafety and the entire scientific community. Establishing and maintaining a biosafety culture is crucial for implementing and accomplishing a biosafety programme. An institutional biosafety policy is a document that describes the scope, purpose and objectives of the biosafety programme. A biosafety policy in place is a demonstration of the prominence of and commitment to biosafety within the organization.

1.2 Assigned Roles and Responsibilities

Although the responsibility for establishing and managing a biosafety programme, including defining and assigning roles and responsibilities, rests with the IBSC of an organization, all facility personnel who conduct R&D or handle or may come into contact with biological agents are responsible for actively participating in the biosafety programme. The DBT Nominee and Biosafety Officer of IBSC have the following crucial responsibilities:

- **DBT Nominee, IBSC**
  - Must ensure compliance with all relevant guidelines and SOPs. The availability of an appropriate containment level and its certification (in the case of BSL-3) should be ensured.
- **Biosafety Officer**
  - Ensures that biosafety measures are in place. The Biosafety Officer is responsible for monitoring the facilities and health of laboratory workers. Develops emergency plans for containment, accidental releases, etc.

For the detailed roles and responsibilities assigned to personnel to successfully manage

a biosafety program, refer to the *"Handbook for Institutional Biosafety Committee (IBSC),"*, as updated time to time and available on IBKP.

1.3 Biosafety Manual

A biosafety manual is a mandatory collection of all the organization-specific documents that describe the foundational elements of their biosafety programme and provides guidance for researchers. This Biosafety Manual provides a summary of pertinent guidelines, policies, regulations, information about safe work practices, safety equipment and personal protective equipment. The manual may include information about supporting programmes and plans, and organization-specific SOPs.

1.4 Biosafety Risk Assessment

The main goal of a biosafety programme is to effectively manage biological risks. An essential activity to achieve this objective is conducting risk assessment, which refers to a systematic qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards. A risk(s) assessment must be conducted based on the known and potential properties of the agents and their relationship to agents that are listed and then placed in an appropriate Risk Group. Genetic engineering can alter/ change the overall risks of an organism on which the engineering is performed. So, re-evaluation of risks associated with the GE organism will be required to assess appropriate risk groups and for the selection of requisite biosafety level facilities. It involves evaluating information to identify hazards, determine the associated risks and develop appropriate risk control strategies that, when implemented, reduce risks to acceptable risks. For more specific information on how to conduct a risk assessment, ***Annexure I*** of this guideline and *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment"*, as updated time to time and available on IBKP may be referred.

1.5 Supporting Programmes and Plans

An effective biosafety program promotes and reinforces safe work practices, improves overall biosafety, increases compliance with applicable regulatory requirements, and supports a culture of biosafety throughout the organization. An important aspect of this programme is the outcomes of biosafety risk assessments, which provide information on risk control measures that are needed to address the identified risks. The correct implementation of these measures must then be managed through the development and management of several supporting programmes or systems. The development and approval of these supporting programmes and plans are usually directed by Laboratory In-charge, with the support of relevant expertise (for example, IBSC members especially Biosafety Officer, engineers, and facility management manpower). The details of these should be readily accessible to researchers and other involved personnel through the biosafety manual, which may include:

- Laboratory access system
- Information on occupational health programme
- Personnel management and training programme
- SOPs development
- Facility design plans
- Laboratory equipment installation and maintenance plan
- Decontamination and disposal system
- Emergency/incident response
- Record management system

- Communication system.

1.6 Implementation of ISO 17025/15189 Standards

ISO/IEC 17025 is the international standard for testing and calibration laboratories. It sets out requirements for the competence, impartiality, and consistent operation of laboratories, ensuring the accuracy and reliability of their testing and calibration results.

Validation of BSL-3 laboratories is to be undertaken by qualified and competent ISO/IEC 17025 accredited organizations. The overall activities, procedures, SOPs and manuals should be made compliant with structured quality management systems. ISO/IEC 15189 specifies requirements for quality and competence in medical laboratories. All BSL-3 laboratories involved in the testing of samples and reporting of results are advised to follow quality control practices and get accreditation as per ISO/IEC 15189 standards in India.

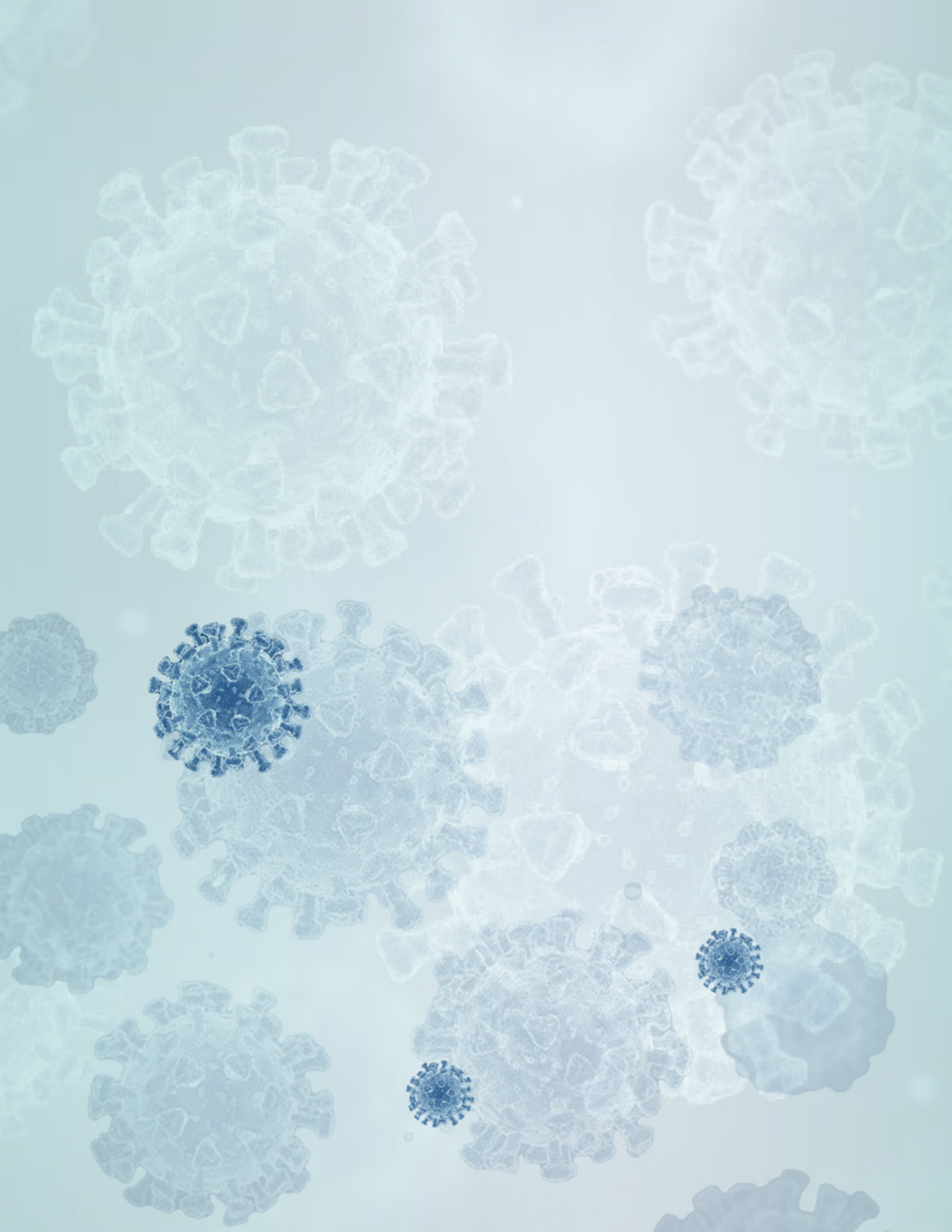
1.7 Implementation of Pathogen Inventory Management System

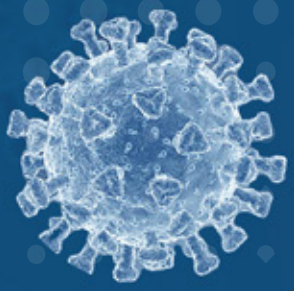
The BSL-3 laboratories involved in pathogen isolation in the laboratory, culture, and archival of RG-3 pathogens should establish a pathogen inventory management system. The defined SOPs should be developed and implemented for practices, procedures and protocols involved in pathogen culture. Every culture stock generated should be documented, monitored and supervised by IBSC. There should be periodic internal as well as external auditing mechanisms in place for the pathogen inventory of the BSL-3 laboratory.

The Biobanking Standard ISO 20387 specifies general requirements for the competence, impartiality and consistent operation of biobanks including quality control requirements to ensure biological material and data collections of appropriate quality. Currently, NABL is in the process to roll out ISO 20387 accreditation, and when available, the BSL-3 laboratories are advised to comply and get accredited for ISO 20387 standard in a phased manner.

1.8 Scientific Ethics

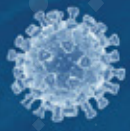
In the recent past, scientific ethics have emerged as a multidisciplinary field with significant implications across scientific community and society. Scientific ethics refer to the ethical framework based on scientific methods and rules, which can be applied to all the fields of science. Ethics provide the focal point for contemporary information, issues, and challenges in the fields of research ethics and scientific integrity. It is aimed at researchers, reviewers, and policymakers to help them pursue the best ways forward in seeking ethics and integrity in all research across disciplines, methods, subjects, participants, and contexts. It is also crucial for the maintenance of research standards and public confidence in science. Therefore, maintaining ethics in scientific research and governance is of paramount importance. This calls for the development of appropriate guidelines, encompassing responsibility of primary researcher, safe laboratory practices, research on humans and human biological materials, use of animals in research, laboratory records, collaborative studies, consultancy work, publication of scientific/technical/biomedical data and results, authorship, redundant publications, plagiarism. On the contrary, scientific misconduct refers to the violation of scientific ethics and code of conduct. It is the responsibility of every organization and individual to uphold their professional integrity, strive to enhance the dignity of the scientific research and take suitable measures to curb professional scientific misconduct.

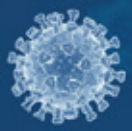




CHAPTER 2

PRINCIPLE AND COMPONENTS OF CONTAINMENT





CHAPTER 2: PRINCIPLE AND COMPONENTS OF CONTAINMENT

2.1 Principle

The principle is the protection of all identified elements (working personnel and community-at-large) from risk(s) posed by organisms (includes risk-inherent in handling high-risk pathogens; GE and non-GE microorganisms, animal, arthropods, aquatic animals, etc.) during their use in the laboratory. In practice, it should be achieved by realization of the three interrelated steps:

- Identification of elements that should be protected: Containment measures should ensure the protection of the laboratory worker(s) (Primary elements) who have maximum possibility of exposure to the organism(s). In addition, the containment measure(s) should also prevent the escape of the organism(s) and, therefore, ensure the protection of the community-at-large and the environment (Secondary elements).
- Identification of potential risk(s) associated with organism(s): It involves assessment of risk(s) associated with the organism(s).
- Identification of containment components to protect identified elements from potential risks associated with the organism

Assessment of the risk:

All the microorganisms are divided into four risk groups (table 1) based on the following:

- Pathogenicity of the organism
- Modes of transmission and host range of the organism
- Availability of effective preventive treatments or curative medicines
- Capability to cause diseases in humans/ animals, and
- Capability to cause epidemics.

Table 1: Risk Group (RG) classification*

Risk Group (RG)	Description
RG 1 (no or low individual and community risk)	A microorganism that is unlikely to cause human or animal disease
RG 2 (moderate individual risk, low community risk)	A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory personnel, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
RG 3 (high individual risk, low community risk)	A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.

RG 4 (high individual and community risk)	A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

*Adopted from the *Laboratory Biosafety Manual, Fourth Edition, WHO, 2020.*

For an updated list of infective microorganisms under different risk groups refer *"List of infective Microorganisms corresponding to different Risk Groups"*, as updated time to time and available on IBKP. Similar lists are available from World Health Organization and CDC; however, the document notified by RCGM, DBT shall be binding.

The risk group of the pathogens coupled with associated factors (Pathogenicity, infectious dose, Natural route of infection, Potential outcome of exposure, pathogen stability, availability of effective prophylaxis or therapeutic interventions) help decide the risk assessment (risk posed) of a particular pathogen. Key steps involved in risk assessment are represented in Figure 1 and important points to be considered during the risk assessment process and risk prioritization matrix are listed in ***Annexure I***.

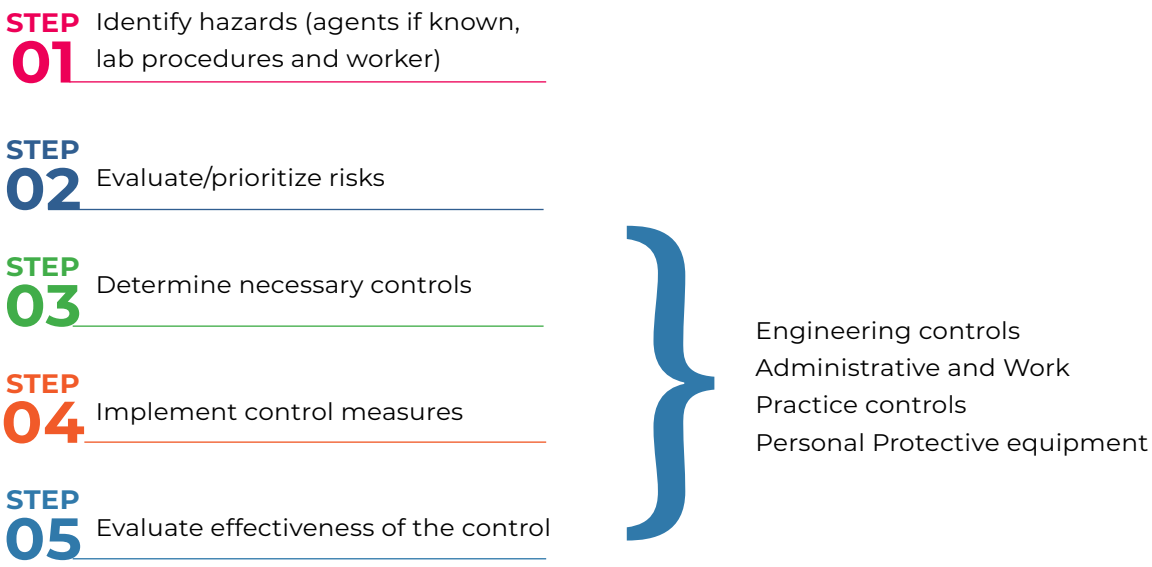


Figure 1: Steps in risk assessment

Identification of containment components: Risk assessment dictates selection of appropriate containment measures or biosafety levels, of which there are four levels (Table 2), for any agent to be handled in laboratories.

Table 2: Relationship of risk group to biosafety levels, practices and equipment

Risk Group	Biosafety Level	Laboratory Type	Laboratory practices	Safety equipment
1.	Basic Biosafety level 1	Basic teaching, research lab	Good Microbiological Techniques (GMT)	None: open bench work
2.	Basic Biosafety level 2	Primary health Services; diagnostic services, research	GMT plus protective clothing, biohazard sign	Open bench plus biological safety cabinet (BSC) for potential aerosols
3.	Containment Biosafety level 3	Special diagnostic services, research	As level 2 plus special clothing, controlled access, directional airflow	BSC, negative pressurized laboratory, double door barrier autoclaves, Eyewash, Shower
4.	Maximum Containment Biosafety level 4	Dangerous pathogen units	As level 3 plus airlock entry, shower exit, special waste disposal	Class III BSC, or positive pressure suits in conjunction with Class II BSCs, double door barrier Autoclave, Filtered air, Eyewash, Shower

As indicated in **Table 2**, the containment strategy encompasses the safe methods (a combination of facilities, practices and procedures) for managing high-risk microorganisms (pathogens) in the laboratory environment where they are being handled or maintained. The principle factors that help achieve the containment levels listed in **Table 2** are described below:

2.2 Physical Containment

The physical containment of the microorganism under study should be able to prevent or minimize its exposure to workers and environment. It is achieved through the use of three elements of containment, i.e., Procedures, Safety equipment(s) and Facility design(s). The protection of personnel(s) and the immediate laboratory environment from exposure to organisms is provided by 'Procedures' and the use of appropriate 'Safety equipment(s)' (Primary containment). The protection of the environment external to the laboratory from exposure to risk-inherent materials is provided by a combination of 'facility design' and operational practices (Secondary containment). The elements are not in the hierarchy and should be used with equal priorities in combination to ensure successful containment.

Procedure

It is emphasized that good laboratory practices (GLP)/ good microbiological techniques (GMT) are fundamental to laboratory safety and cannot be replaced by other means, which can only supplement it. The following must be followed by workers involved in the research in handling of organism(s) in consideration of the following:

- Strict adherence to standard microbiological practices and techniques, selection of laboratory practices as required for ensuring safety, awareness of potential hazards

- Providing/arranging for appropriate training of personnel.

Safety Equipment

The Laboratory In-charge, in consultation with IBSC, should ensure that adequate equipment is provided and used properly. In selecting safe laboratory equipment, the general principles that should be considered include:

- Designed to limit or prevent contact between the operator and the infectious organisms.
- Constructed of materials to ensure that these are impermeable to liquids, corrosion-resistant and meet structural strength requirements.
- Fabricated to be free of burrs and sharp edges.
- Designed, constructed and installed to facilitate simple operation and to provide ease of maintenance, accessibility for cleaning, and ease of decontamination, testing and validation.

Safety equipment broadly includes

- Instruments like Biological Safety Cabinets (BSC), autoclave and a variety of enclosed containers (e.g., safety centrifuge cup).
- Personal protective equipment (PPE) such as gloves, coats, gowns, shoe covers, boots, respirators, face shields, safety glasses, etc.

Detailed performance and construction specifications that are required to ensure that the equipment possesses necessary safety features are detailed in ***Annexures II - IV.***

Facility Design

The design of the facility is important in providing a barrier to protect not only person working in the facility but also outside of the laboratory and the community from infectious organisms which may be accidentally released from the laboratory. Special consideration should be given to the following conditions:

- Creation of aerosols.
- Work with large volumes and/or high concentrations of microorganisms.
- Overcrowded, over equipped laboratories.
- Infestation with rodents or insects.
- Unauthorized entrance.

2.3 Biological Containment

Biological containment employs strategies that render an organism used for genetic engineering either incapable of survival or severely reduce its ability to survive or reproduce in the open environment. Such GE organisms would either remain viable only under the selective environmental conditions for which they were designed for or would carry self-contained mechanism(s) that could be induced when the need arises to eradicate such GE population. In addition to physical containment, such biological containment consequently ensures additional safety while working with GE organisms and provides more flexibility of handling organisms with higher risk(s).

It is always advisable to consider biological containment strategies especially if the final aim of the experiment is to release the organisms into the environment. In doing so, it is the responsibility of the Principal Investigator to first identify the possible risk(s) associated with the host, vector and modification(s) proposed and select appropriate strategies to reduce or limit:

- The risk(s) associated with the host organism.
- The infectivity of vector to specific hosts.

- The host-vector survival in the environment.

2.4 Laboratory Monitoring

Laboratory monitoring is a systematic, regular and preventive activity designed for corrective actions, if required. It is the responsibility of the Laboratory In-charge to ensure:

- Prevention of any unauthorized entry in the laboratory.
- Only allow entry of persons properly trained in laboratory safety.
- Personnel should be advised of special hazards and be required to know and follow standard practices and procedures. Such instructions should be prominently displayed near the entrance of the laboratory/facility.
- Persons at increased risk(s) of acquiring an infection or for whom infection may have unusually serious consequences (e.g., Immuno-compromised, Women during pregnancy, etc.) are informed of their risk(s) and should be restricted from entering the laboratory.
- To create a friendly environment where workers follow proper containment strategies and are fearless to report violations of the procedure(s), identify co-worker failings, express concerns and offer suggestions.
- Personnel should maintain Log books of instruments used and records of breakdown of instruments and installations.
- All safety equipment is working properly and if not, maintenance of the equipment is done immediately. All civil structures are in good condition to ensure proper containment.
- A regular housekeeping schedule is maintained.
- Prevention of diseases in the general or occupational environment.
- Documentation of daily laboratory activity for immediate consideration of emergency procedures in cases of breach in containment.
- Proper documentation of work involving both non-GE and GE organisms in the same facility should be maintained to ensure that no unintentional cross-contamination of non-GE organisms occurs.
- Stringency in monitoring procedure(s) must be determined based on the biosafety level of the laboratory and should be determined by the Laboratory In-charge with consultation of scientific experts.
- Further the procedures mentioned in the *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment"*, as updated time to time and available on IBKP should be strictly complied.

2.5 Health and Medical Surveillance

Medical surveillance is of paramount importance for personnel working in high-containment facilities. It enables to assess the health problems that may occur in the workplace by analysis of health information. It provides a mechanism for targeted prevention of health problems. The objectives of the health and medical surveillance of laboratory personnel are:

- Testing and continuous monitoring of the fitness of individuals authorized to work in a containment laboratory
- Prevent individuals from acquiring an infection during the work.
- Early detection of laboratory-acquired infection.

- Assessing the efficacy of protective equipment and procedures
- Ensure prophylactic vaccinations where needed and monitor booster regimens and assessment of seroconversion, as applicable.

2.6 Decontamination and Disposal

The safe disposal of hazardous waste is of utmost importance in BSL-3 labs. Decontamination and disposal in laboratories are closely interrelated acts, since disinfection or sterilization constitutes the first phase of disposal. All infectious waste from BSL-3 laboratories should be decontaminated before removal for off-site disposal. BSL-3 labs must be equipped to decontaminate laboratory waste using an appropriate method of decontamination, depending on the biological risk assessment. Steam autoclaving is the preferred method for all decontamination processes. Compliance with relevant regulations and guidelines is essential when disposing of hazardous materials. The decontamination and disposal procedures mentioned in the *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment",* as updated time to time and available on IBKP should be strictly complied with. Also, all the decontamination and disposal processes should comply with the guidelines of the Central Pollution Control Board. Proper storage, transport, and treatment of waste should be implemented to protect human health and the environment.

2.7 Emergency Procedures

Emergency contingency plans should be prepared for each laboratory and institution, considering every possible breach in biocontainment. These are best prepared by the Laboratory In-charge in conjunction with his/her staff, Biosafety Officer and IBSC. This procedure offers the best prospect of success as it is the immediate staff that is most familiar with the hazards associated with the particular laboratory. Once the emergency plan is formulated, it should be displayed in a conspicuous place in the laboratory for immediate reference. Statutory rules and regulations for each of these will normally be laid down by the competent national or local authorities. Their assistance and guidance should be sought if necessary. The emergency procedures mentioned in the *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment",* as updated time to time and available on IBKP should be strictly complied with.

2.8 Training

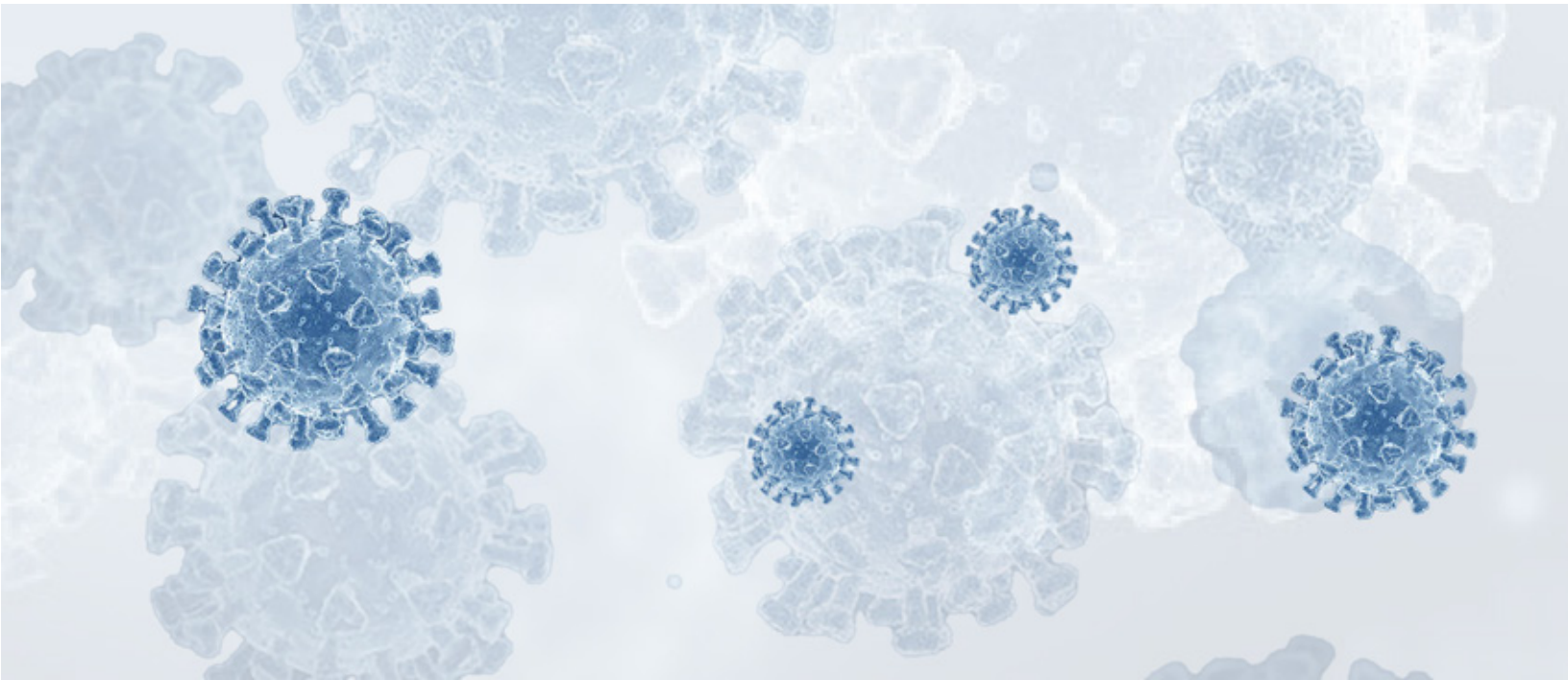
Personnel training in biosafety is the key for prevention of laboratory-acquired infections, incidents and accidents ensuring success of any containment strategy. Based on the organism to be handled and the nature of work, the training program is to be developed and the Laboratory In-charge must play the key role in training of laboratory staff.

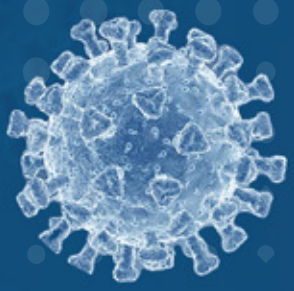
A training program must include information on the safe handling of organisms of different risk groups that are commonly handled by all laboratory personnel, involving any possible exposure scenarios and decontamination and emergency plan strategies. Training should involve classroom work as well as significant one-on-one mentoring in the lab before an individual is allowed to work alone. It may include:

- Inhalation risk(s) (i.e., aerosol production), such as using loops, streaking agar plates, pipetting, making smears, opening cultures, taking blood/serum samples, centrifugation etc.
- Ingestion risks, such as handling specimens, smears and cultures.
- Risk(s) of percutaneous exposures, through the use of syringe and needle techniques.

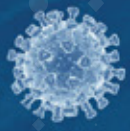
- Animal handling that may result in bites and scratches.
- Handling of blood and other potentially hazardous pathological materials.
- Decontamination and disposal of infectious material.
- Emergency procedures in case of unwanted breach in containment.

Strict training is mandatory before the authorization of any new worker in the laboratory and the work must be done under stringent safety conditions. The facility personnel must be trained in the equipment and procedures used in the facility. The facility personnel should be provided training on the operation, servicing and maintenance of all engineering installations and handling of emergencies due to engineering system failures, fire etc. Records of the training must be kept and made available to the regulator if requested. Refresher training courses, both theoretical and practical, need to be conducted annually or as and when required, in case of any modification or change in any integral system of containment.

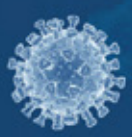




CHAPTER 3



ESTABLISHMENT OF BIOSAFETY LEVEL 3 (BSL-3) FACILITY



CHAPTER 3 ESTABLISHMENT OF BIOSAFETY LEVEL 3 (BSL-3) FACILITY

Biosafety Level 3 (BSL-3) applies to clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through the direct contact, fomites or inhalation route of exposure. The decision to establish a BSL-3 lab should be based on a proposed scientific work plan with clearly defined objectives (routine diagnosis, research, animal experimentations, production or teaching etc.) and its subsequent risk assessment. The BSL-3 containment facility requires strengthening the operational and safety programmes over and above those for basic laboratories. The entire process of establishing a BSL-3 lab can be split into the following steps for ease of implementation:

3.1 Objectives and Scope of work

The basic objective for the establishment of a containment laboratory is to ensure Biosafety, that is, creating a safe environment for detection, identification, propagation and manipulation of risk-inherent microorganisms/GE organisms in the laboratory, to ensure safety and health of research personnel as well as that of the community and the environment. The scope of the work to be carried out in the envisaged BSL-3 facility must be clearly identified and defined, usually:

- Conducting basic, applied or clinical research or a combination of these on high-risk pathogens
- Handling clinical samples of patients infected with high-risk pathogens during routine diagnostic testing or outbreaks.

The scope decides the design of the BSL-3 lab, total work area, bench space, number of BSCs to be installed, area of pathogen/ sample repository, supporting area etc. The scope along with the Biorisk assessment and management plan shall be drafted by the Laboratory In-charge in consultation/ collaboration with the Institutional Biosafety Committee. The *"List of Infective Microorganisms corresponding to different Risk Groups",* as updated time to time and available on IBKP; shall be referred to while considering scope of work to be carried out in a BSL-3 facility. The facility must undergo verification that the design and operational parameters have been met prior to operation. All the activities involving handling of infectious agents should be performed as per the pre-defined laboratory specific SOPs. Proper thought should be given to ensure sufficient utilization of such a facility given the cost of establishment and maintenance of this facility.

3.2 Pre-requisites for the construction

An important pre-requisite of the BSL-3 facility is the site selection and determination of risk assessment of the site conditions based on the objectives and scope of proposed work. BSL-3 laboratory should be ideally located in a standalone building or it shall be separated from the general traffic flow i.e., regular buildings including administration, library, etc., that are frequently visited by employees or public. Access to the building should be strictly restricted and only authorized persons should be allowed access through an anteroom/airlock facility, preferably controlled through electronic systems including surveillance systems with a provision for

a 3-tiered security system built within the building. The construction site should meet the basic criteria of an uninterrupted supply of water and electricity and should provide easy connectivity to the nearest airport. Geographical and climatic conditions, such as geological fault lines, or extreme heat, cold or humidity may affect the laboratory design. Therefore, an in-depth risk analysis based on geographical data of the designated site should be carried out in the area selected, for susceptibility to natural disasters like landslides and earthquakes. The civil structure should be designed as earthquake-resistant in accordance with provisions of IS1893 as per the relevant seismic zones. If an existing structure is to be converted to BSL-3 lab, then suitability of structure as per existing provisions of the above code should be thoroughly checked. In case of any deficiency, retrofitting should be undertaken. In addition special care should be taken to ensure safety of lab during seismic movements. The proposed site should be away from high tension electric lines to avoid any related accidents. The risk of possible damage to the site from heavy rains and flooding should also be systematically evaluated. The proposed site should be subjected to soil testing to detect possible presence of borehole logs', type of soil, strength of soil to bear load of structure, compaction of soil, chemicals present in soil, moisture content, water table etc

Contemplating the above, the conceptual proposal for BSL-3 laboratory with detailed drawings and plans, justifying the objectives for the construction as per the requirements while abiding with the national guidelines on biosafety and biosecurity, should be postulated. This involves preparing a detailed flowchart of the construction work and a schematic drawing to enable detailed planning. The drawings must depict the layout of all laboratory areas to facilitate placement of essential on-site and stand-alone equipment (including autoclaves, biological liquid effluent decontamination plant/chemical kill tank, air handling units, exhaust filters). The plan should also indicate the placement of safety equipment within the facility, such as fire extinguishers, water sprinklers etc. A detailed concept proposal with detailed drawings, plans as per requirements should be formulated. Qualified and experienced architects-engineers should be involved in designing the facility. Strict monitoring should be done for proper facility construction and in a time-bound manner until the facility is validated and handed over to the institution.

3.3 Pre-design considerations for BSL-3 facility and design of the lab

Several criteria should be considered while conceptualizing and designing a BSL-3 lab. The laboratory design must ensure greater sustainability while maintaining an appropriate control of biosafety. This includes a large set of strict and complicated operational practices, safety equipment and facility design criteria for maximum containment measures.

Defining the workflow and preparation of flow charts based on scope along with the utility of the BSL-3 laboratory plays a primary role in choosing a model and design of the BSL-3 lab. Multiple designs of BSL-3 laboratories exist, varying in the overall layout, area, infrastructure and cost input (representative BSL-3 drawings are shown in ***Annexure IX***). In any format, these laboratories are sophisticated, expensive establishments, and the choice of the design depends on several factors: the overall mandate, objectives and scientific framework of the laboratory, the frequency of occurrence of high-risk pathogens in the region, clinical-scientific, administrative and financial commitment, availability of expertise, laboratory space and funding support. The features of the different types of BSL-3 laboratories are summarized in **Table 3**. Whatever be the facility design, the

features listed below are core requirements for biosafety for all laboratories handling biological agents and these must be considered while designing the lab:

- Ample space must be provided for the safe conduct of laboratory work and for cleaning and maintenance.
- Designated hand-washing basins operated by a hands-free mechanism must be provided in each laboratory room, preferably close to the exit door.
- The laboratory must be a restricted-access area. Laboratory entrance doors should have vision panels (to avoid accidents during the opening), appropriate fire ratings and should preferably be self-closing.
- Doors must be appropriately labelled with the international biohazard warning symbols wherever biohazardous materials are handled and stored.
- Laboratory walls, floors and furniture must be smooth, easy to clean, impermeable to liquids and resistant to the chemicals and disinfectants normally used in the laboratory.
- Laboratory bench tops must be impervious to water and resistant to disinfectants, acids, alkalis, organic solvents and moderate heat.
- Laboratory furniture must be fit for purpose. Open spaces between and under benches, cabinets and equipment must be accessible for cleaning.
- Laboratory lighting (illumination) must be adequate for all activities. Daylight should be utilized effectively to save energy. Undesirable reflections and glare should be avoided. Emergency lighting must be sufficient to permit safe stopping of work as well as safe exit from the laboratory.
- Laboratory ventilation where provided (including heating/cooling systems, especially fans/local cooling split-system air conditioning units – specifically when retrofitted) should ensure airflows do not compromise safe working.
- Consideration must be given to resultant airflow speeds and directions, and turbulent airflows should be avoided; this also applies to natural ventilation.
- Laboratory storage space must be adequate to hold supplies for immediate use to prevent clutter on bench tops and in aisles. Additional long-term storage space, conveniently located outside of the laboratory room/space, should be considered.
- Space and facilities must be provided for the safe handling and storage of chemicals and solvents, radioactive materials, and compressed and liquefied gases if used.
- Facilities for storing food and drink, personal items, jackets and outerwear must not be provided inside the laboratory.
- Facilities for eating and drinking must not be provided inside the laboratory
- First-aid facilities must be readily accessible and suitably equipped/stocked.
- Appropriate methods for decontamination of waste, for example, disinfectants and autoclaves, must be available in proximity to the laboratory.
- The management of waste must be considered in the design. Safety systems must cover fire, electrical emergencies and emergency/incident response facilities based on risk assessment.
- There must be a reliable and adequate electricity supply and lighting to permit safe exit.
- Emergencies must be considered in the design as indicated in the local risk assessment and should include the geographical/meteorological context.
- Fire security and flood risk must be considered.
- All installations must be securely fastened.

Table 3: Types of BSL-3 laboratories and secondary barrier requirements

Facility Type (Areas of Utilities)	Primary Containment	Eye-wash	Hand wash	Wet Shower	On-site Autoclave	Ventilation 100% Fresh air	Ventilation Recirculatory (30% Fresh air)	Air changes /Hr. [ACPH]**	Effluent Decontamination System	
									Chemical Type	Steam Type
BSL-3, Type-1 (Basic laboratory for laboratory diagnosis [serological & molecular] for RG-3 known public health disease agents)	Class II A2	M	M	NM	NM [vertical autoclave may be considered]	M*	NA	8-12	M*	NA
BSL-3, Type-2 (Laboratory with facility for propagation of infectious agents in vitro & in vivo for RG-2 agents) + equipped for providing diagnosis for MDR & X-TB	Class II A2	M	M	NM*	NM [vertical autoclave may be considered]	M	NA	8-12	M*	NA
BSL-3, Type-3 (Laboratory for laboratory diagnosis and with mandate of in vitro propagation of specific infectious agents for RG-2 related to DNA recombination technologies or RG-3 / MDR & X-TB agents)	Class II A2	M	M	NM*	NM [vertical autoclave may be considered]	M	NA	8-12	M*	
BSL-3, Type-4 (Laboratory for laboratory diagnosis and with mandate of in vitro and in vivo propagation of specific infectious agents for RG-3 related to DNA recombination technologies or RG-3 /MDR & X-TB agents). Animal with experimentation with RG-3 agents up to mice, chickens and rodents.	Class II A2 + IVC	M	M	M	NM [vertical autoclave may be considered]	M	NA	8-12	NA	M

BSL-3, Type-5 (Laboratory for laboratory diagnosis and with mandate of in vitro and in vivo propagation of specific infectious agents for RG-3 related to DNA recombination technologies or RG-3 /MDR & X-TB agents). Animal with experimentation facility with RG-3 agents equipped with animal challenge experimentation with RG-3 agents	Class II A2 + IVC	M	M	M	NM [vertical autoclave may be considered]	M	NA	10-12	NA	M
ABSL-3, (Laboratory for vector biology experimentation and for the surveillance of agents of vector-borne diseases of RG-3 level or dealing with arthropods with infectious agents for RG-2 level related to DNA recombination technologies with facility to maintain small animals for experimentation facility with RG-3 agents)	Class II A2 + IVC	M	M	M	NM [vertical autoclave may be considered]	M	NA	10-12	NA	M

* Preferred, however depends on risk assessment for mandated work

** Air Changes depend on risk assessment for mandated work

NA: Not Applicable

NM: Not Mandatory, depends on risk assessment for mandated work

M: Mandatory

NB:

a. If the mandate of the laboratory includes processing & propagation [in-vitro and in-vivo (in small animal model)] of samples from known or unknown high-risk group agents' outbreak/unusual outbreaks: it is advised to follow BSL-3, Type-5 standards. However, if the mandate of the laboratory includes processing & propagation [in-vitro & in-vivo] of unknown samples from known or unknown high-risk group agents' outbreak/ unusual outbreaks for vector biology experimentation: it is advised to follow ABSL-3 standards.

b. Laboratories working with virus culture only, may use validated chemical disinfection protocol in the ETP. Laboratories working with spore-forming bacteria, fungi and other infectious agents must follow steam-based disinfection protocol. For solid waste and liquid effluent treatment, steam-based disinfection protocol may be considered following proper validation.

3.4 Construction of the BSL-3 laboratory

The BSL-3 laboratory has special engineering and design features. The technical standards for the engineering controls with respect to special safety practices, equipment, and facility requirements that apply to BSL-3 have been detailed in ***Annexure II***. The following features should be given added consideration while constructing a BSL-3 lab:

- The anteroom should have facilities for separating clean and dirty clothing.
- Anteroom doors shall be self-closing and interlocking so that only one door is open at a time. A break-through panel may be provided for emergency exit use.
- Surfaces of walls, floors and ceilings should be water-resistant and easy to clean. Openings through these surfaces (e.g., for service pipes) should be sealed to facilitate the decontamination of the room(s).
- The laboratory room must be sealable for decontamination. The air-ducting systems must be leak-proof (sealed) and constructed to permit gaseous decontamination.
- Windows must be closed, sealed and break-resistant.
- A hand-washing station with hands-free controls should be provided near each exit door.
- Provision for a sensor-based or foot / elbow-operated eye wash station should also be there.
- There must be a controlled ventilation system that maintains a directional airflow into the laboratory room. A very vital aspect of BSL-3 design and operation is the maintenance of negative pressure in the core facility where infectious pathogen(s) is/are to be handled. The supply and exhaust components of the ventilation system must be designed to maintain the laboratory all the time under negative pressure as compared to surrounding areas and provide differential pressure or directional airflow, as appropriate, between adjacent areas within the laboratory. A dedicated non-recirculating, high-efficiency particulate air (HEPA) filtered, ventilation system should be provided. A heating, ventilation and air-conditioning (HVAC) control system shall be installed to prevent positive pressurization of the laboratory. A visual monitoring device with or without alarm(s) should be installed so that staff can at all times ensure that proper directional airflow into the laboratory room is maintained. Consideration should be given to the installation of audible or visible alarms to notify personnel of HVAC system failure.

- All HEPA filters must be installed in a manner that permits decontamination and testing.
- Biological safety cabinets should be placed/positioned away from walking areas and out of crosscurrents from doors and ventilation systems.
- The exhaust air from Biological Safety Cabinets, which has passed through HEPA filters, must be discharged in such a way as to avoid interference with the air balance of the cabinet or the building exhaust system.
- An in-situ, double-door barrier autoclave for the decontamination of contaminated waste material should be available in the containment laboratory.
- Backflow-prevention devices must be fitted to the water supply. Vacuum lines should be protected with liquid disinfectant traps and HEPA filters, or their equivalent. Alternative vacuum pumps should also be properly protected with traps and filters.
- The BSL-3 facility design, operational parameters, and procedures must be validated and documented prior to operation. Facilities must be re-validated and documented at least annually.
- The entry/exit should be through cloth change and additionally, through shower room while exiting. The need and number of showers shall be as per the laboratory SOP and requirement which in turn is guided by the risk assessment.
- There should be an additional personnel change room contiguous with shower, depending on type of work in BSL-3 facility
- BSL-3 must have a barrier steam Autoclave and fumigation chamber. Material supplies and equipment shall enter/exit through double-door barrier Autoclave/ Fumigation chamber or Air Lock.
- All vent lines must be protected by HEPA filters.
- Pressure gradient in the direction of more contamination with more negative pressure required.
- Air supply duct and exhaust duct within the contaminated BSL-3 lab should be air tight and preferably made of stainless steel. Duct material should be fumigation friendly. Duct must be tested for leakage by pressure decay test.
- All supply and exhaust air dampers should be airtight and tested before installation. The complete laboratory should be in situ tested for any leakage before commissioning by pressure decay test.
- All entry/exit gates should be airtight and gates must be tested for air leakage before installation and on an annual basis thereafter by pressure decay test or soap bubble leak test.
- BSL-3 laboratory area must have 8 - 12 air changes per hour. ABSL-3 and other highly contaminated areas of the laboratories like post-mortem room should have a minimum 10-12 air changes per hour.

While civil work is ongoing, the procurement of equipment and personal protective equipment needs to be planned, ensuring the following:

3.4.1 Laboratory equipment

Equipments are an integral part of the BSL-3 laboratory for the conduct of experiments/ procedures. Based on the workflow and the flow charts prepared for the conduct of tests, the equipment required for specific work needs to be identified. At Biosafety Level 3, manipulation of all potentially infectious materials must be conducted within a biological safety cabinet (Class-II or Class-III, based on risk assessment) or other primary containment device. In addition:

- Autoclave size and configuration shall be based on the program/laboratory's needs. Sterilization/ decontamination cycles and options are program driven. Autoclave integrated with the containment barrier of the BSL-3 laboratory shall provide bio-seal. Boiler facility may be required if autoclaves operate on steam.
- Consideration should be given to equipment such as centrifuges, which will need additional containment accessories, for example, safety buckets or containment rotors.
- Equipment that may produce infectious aerosols must be contained in primary barrier devices that exhaust air through HEPA filtration or other equivalent technology before being discharged into the laboratory or outside.
- Laboratory equipment should be routinely decontaminated, as well as, after spills, splashes, or other potential contamination, as per the SOPs.
- Dunk Tanks and Pass Boxes: their size and location shall be determined by the program and shall be integral to the containment barrier. The depth of partition must exceed the expected maximum pressure differential.
- Equipment like centrifuges, cell-sorters for use with infected cells; may need additional local exhaust ventilation with HEPA filtration for efficient containment.
- Other equipment and accessories required for environment protection and personal protection should also be listed for pre-design preparation i.e.: use of HEPA filtration of exhaust air and chillers for HVAC, effluent decontamination or chemical kill tank, personnel shower in the changing area, inner and outer change rooms for showers to allow easy entry and exit protocols for the laboratory personnel.
- Individually Ventilated Cages (IVC) shall be used for housing laboratory animals, as and when required. CPSEA guidelines need to be adhered for determining the size of IVC.

3.4.2 Personal Protective Equipment

Personal Protective Equipment (PPE) is specialized clothing or equipment worn by laboratory workers in BSL-3 facilities to protect against a hazard (e.g., infectious agents and toxins). PPE ranges from basic protective equipment such as safety glasses or goggles, gloves, lab coats, gowns, shoe covers or as complex as a Biosafety Level 4 "positive pressure suit", which includes the use of a positive pressure suit connected to a HEPA filtered airline, that completely isolates the facility personnel from the laboratory environment, ensuring there is no contact with the potentially hazardous material. A thorough risk assessment based on the characteristics of the infectious agent or toxin being manipulated and the type of laboratory procedures performed will determine the type of PPE required. Some of the considerations for PPE use in a BSL-3 facility are as follows:

- The use of laboratory coats, gowns or uniforms is required to prevent contamination of street clothing. Getting naked protocol may be followed, if deemed necessary, before entering the containment area. The laboratory design and infrastructure should be compliant for its implementation. Laboratory scrub suits should be worn within the PPE, PPE should be front-closed and coverall type.
- Goggles and face protection shields must be used when there is a potential for splashes of microorganisms or other hazardous materials.
- Face mask and appropriate gloves should be worn as protection for all procedures

and replaced/discarded frequently after handling infectious microorganisms

- It is preferable to use two layers of gloves while experimenting and outer layer should be disposed of immediately after working at BSC.
- All PPE should be removed while exiting BSL-3 lab so that the transfer of infectious materials to areas beyond is minimized.
- Used disposable PPE should be disposed of with other contaminated waste and reusable PPE (i.e., goggles) should be appropriately decontaminated after use and before reuse.
- Reusable protective clothing should not be taken outside the laboratory. The contaminated protective clothing should be placed in a biohazard bag and autoclaved onsite before laundry.

3.5 Commissioning of the laboratory

Commissioning is the verification of physical construction with the design parameters/ predetermined performance criteria, and it is one part of the overall validation process. Before the laboratory is taken over after construction, each element, as per layout, needs to be commissioned and tested to ensure safe facility operation. This requires verification and documentation of critical containment components, equipment start-up, adjustments of parameters, control system calibration, balancing and performance testing.

The commissioning procedure for the laboratory should be well designed and implemented to verify the safe aspects of facility operation. Commissioning of facility shall include all critical elements such as airflow patterns, negative pressures in different zones of the facility, biosafety cabinets, temperature profiles in autoclaves, procedures for decontamination and sterilization, verification of light lux level, operation of HVAC systems, measurement of chilled water pumps capacity, air quantities at outlet diffusers/grilles, air compressor capacity, air curtains, steam boiler, clean room garment storage cabinet, floor traps, drains, dunk tanks, checking of ceiling panels, pass box, shower cabinets/ air shower, water outlets, air leak in ducts as well as plenums, doors and view panels along with functioning of all the alarm systems.

Additionally, commissioning of all the basic requirements as per the approved layouts, including electrical connections, emergency electric supply, UPS, local area network (LAN) connections, servers, water connections, sewage connection, hardware fitting, telephones and intercoms is to be ensured. Functioning of the BMS with all the desired parameters, fine setting of access control and all the inventories, etc. is to be done.

Essential tests to be conducted during commissioning are enlisted in ***Annexure III***. Testing of equipment/critical components should be initially performed by the construction contractor in the presence of the team involved, and test results should be properly documented. All performance parameters and adjustments/replacements, if any, carried out during testing should be documented for future reference. Functioning of all critical parameters should be repeated and demonstrated to IBSC, in presence of the Laboratory In-charge. Final testing and commissioning should take place in presence of an Expert Committee constituted for the purpose, comprising of Scientists experienced in working/ establishing BSL-3 laboratory, Engineers experienced in establishing/maintaining BSL-3 laboratory and Representative of CPCB.

3.6 Validation of the laboratory

Validation represents the successful

completion of commissioning and acceptance of operational protocols that meet the required design parameters, as per these guidelines. The validation of the containment facility is a documented process, which serves not only to verify the proper functioning of all four controls (Administrative, Engineering, Workplace practices, PPE) during normal operation but also to ensure biosafety and biosecurity in the event of a failure of any of these controls.

Validation of the BSL-3 facility should be conducted by qualified and competent ISO/IEC 17025 accredited organizations; in presence of Expert Committee constituted for the purpose, comprising of Scientists experienced in working/establishing BSL-3 laboratory, Engineers experienced in establishing/maintaining BSL-3 laboratory and Representative of CPCB. The validation process aims to ensure biosafety and biosecurity of the workers and the surrounding environment as well as adherence to biosafety regulations of the country. Performance-based tests to be conducted at the time of validation are provided at ***Annexure IV***. Approvals from all concerned statutory bodies like fire safety, municipal corporation, pollution control board, electrical inspector, natural climatic safety and boiler inspection authority, etc., as applicable, must also be available and verified. Approvals from IBSC/RCGM/DBT/ Controlling Ministry are also to be ensured.

The validation process should also verify that the following documents have been developed in the facility and are available:

- A document describing the mandate and features of the laboratory
- A technical/operation manual explaining the maintenance and operation of engineering systems of the facility while addressing biosafety aspects
- Bio-safety manual
- Personnel training and competence
- SOPs for working in the facility
- Mock drill has been conducted.

3.7 Operation and maintenance of the laboratory

Risk assessment and risk management to ensure biosafety and biosecurity are central dogma for working in a BSL-3 lab. To ensure safe and efficient working in the BSL-3 facility, SOPs as exemplified in ***Annexure V***, must be prepared and made available to all personnel working in the facility. This aspect ensures that the lab runs without compromising biosafety and biosecurity by having contingency plans for repairs, annual maintenance contracts and assurance of an uninterrupted supply of spares as and when required. The following are the integral features of the operation and maintenance:

3.7.1 Code of practice

The code of practice for basic laboratories applies except where modified, for example, as follows:

- In addition to the international biohazard warning symbol and sign, the laboratory access doors must identify the biosafety level and the name of the Laboratory In- charge who controls access and indicate any special conditions for entry into the area, e.g., Immunization. Facility personnel must be vaccinated as per the scope of work in the facility.
- The Laboratory In-charge must enforce the institutional policies that control access to the laboratory.
- Laboratory protective clothing must be of the type with solid-front or wraparound gowns, scrub suits, cover-alls, head covering and dedicated shoes.
- Front-buttoned standard laboratory coats

are unsuitable, as are sleeves that do not fully cover the forearms. Laboratory protective clothing must not be worn outside the laboratory, and it must be decontaminated before it is laundered.

- Open manipulations of all potentially infectious material must be conducted within a biological safety cabinet.
- Respiratory protective equipment may be necessary for some laboratory procedures.
- A laboratory-specific biosafety manual must be prepared and adopted. The biosafety manual must be readily available and accessible.
- The Laboratory In-charge must ensure that laboratory personnel demonstrate proficiency in standard and additional microbiological practices before working with BSL-3 agents.

3.7.2 Personnel competence and training

In addition to engineering controls, as described in detail above, an integral aspect of risk management is the competence, training and experience of the Principal Investigator (PI)/Laboratory In-charge and its staff in being proficient at working in BSL-3 laboratory.

There must be provisions to train every new BSL-3 laboratory worker in biosafety and protection standards by undergoing theoretical and hands-on practical training. Theoretical training helps laboratory workers develop an understanding of the underpinnings of biocontainment operations and the laboratory systems that support these operations. Hands-on practical training includes:

- A comprehensive orientation to the specific facility in which the person will work to include a complete review and documented understanding of all the standard operating procedures
- An orientation to engineering aspects of the facility
- An overview of all safety procedures, including alarms and emergency operations
- Information on variations in appropriate levels of protective equipment depending on the risks of the research conducted, along with an introduction to the care and use of a protective suit or glove box.

At the end of such training, the new worker should be able to demonstrate to the PI/ Laboratory In-charge their proficiency in safely and competently functioning in a BSL-3 laboratory, including donning and doffing PPE and performing some routine procedures (possibly using lower-risk RG-2 biological materials or mock inconsequential non-infectious materials) while wearing required PPE, including respiratory protection. Such hands-on proficiency training, mentorship, and didactic training are critical for evaluating and establishing the researcher's ability to work in a high-containment laboratory. The final decision on when a person is allowed independent access is subjective and based on an assessment by the Principal Investigator and Laboratory In-charge. It is usually after the person has had extensive experience working in the facility. The time required to gain full independent access may also vary depending on the kind of work the person will be undertaking. There should be constant and continuous monitoring and training by experts to improve laboratory skills and develop an awareness of laboratory workers of current biosafety issues. This may be done on an annual basis.

In addition to researchers, a variety of individuals - administrators, support staff, equipment service personnel, and in certain situations, emergency responders need

access to high-containment laboratories. They all should be provided with realistic information about the hazards that exist in the high-containment facility and should be given some level of training before gaining access to a BSL-3 lab. Similarly, appropriate members of the community in the immediate vicinity must be appraised of the same so as to help guide their response(s) in an emergency.

3.7.3 Health and Medical Surveillance

Each BSL-3 lab worker should be medically fit to work in this lab. The medical fitness should be certified by the Biosafety Officer of the IBSC. The objectives of health and medical surveillance programs for Biosafety Level-2 also apply to containment laboratories, that is, Biosafety Level-3, except where modified as follows:

- Medical examination of all laboratory personnel who work in containment laboratories – Biosafety Level -3 is mandatory. This should include a recording of a detailed medical history and an occupationally-targeted physical examination.
- After a satisfactory clinical assessment, the examinee may be provided with a medical contact card stating that he or she is employed in a facility with a containment laboratory – Biosafety Level-3. This card should include a picture of the cardholder, and always be carried by the holder. The name(s) of the contact persons to be entered will need to be agreed upon locally but might include the Laboratory In-charge, Medical Officer and/or Biosafety Officer. A template for the Medical Card is provided in *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment"*, as updated time to time and available on IBKP.

3.7.4 Emergency/Incident Procedures

Any unforeseen incident/breach in containment must be immediately reported to the regulatory authorities. The Laboratory In-charge and Biosafety Officer must be immediately informed. The IBSC must be informed about the emergency and response procedure. The IBSC must bring such incidents to the notice of RCGM/GEAC. All such instances shall be duly recorded and reported. In addition to emergency procedures, containment laboratories require additional considerations. These include:

Puncture wounds, cuts and abrasions

- The affected individual should remove protective clothing, wash the hands and any affected area(s), apply an appropriate skin disinfectant, and seek medical attention as necessary.
- The cause of the wound and the organisms involved should be reported, and appropriate and complete medical records kept.

Ingestion of potentially infectious material

- Protective clothing should be removed and medical attention sought.
- Identification of the material ingested and circumstances of the incident should be reported, and appropriate and complete medical records should be kept.

Potentially infectious aerosol release (outside a biological safety cabinet)

- All persons should immediately vacate the affected area and any exposed persons should be referred for medical advice.
- The Laboratory In-charge and the Biosafety Officer should be informed immediately.
- Signs should be posted indicating that

entry is prohibited.

- No one should enter the room for an appropriate amount of time (minimum 1h), to allow aerosols to be carried away and heavier particles to settle.
- After this, decontamination should proceed, supervised by the Laboratory In-charge and Biosafety Officer. Appropriate protective clothing and respiratory protection should be worn during the decontamination procedure. The facility may be allowed for re-entry only after it is cleared and approved.

Broken containers and spilled infectious substances

- Broken containers contaminated with infectious substances and spilled infectious substances should be covered with a cloth or paper towels.
- Disinfectant (as per laboratory SOP) should then be poured over these and left for the appropriate amount of time. The cloth or paper towels and the broken material can then be cleared away.
- The contaminated area should then be swabbed with disinfectant.
- All the materials assisting decontamination should be autoclaved or placed in an effective disinfectant.
- Gloves must be worn to protect hands from exposure to hazardous materials. Glove selection should be based on an appropriate risk assessment. For example, Neoprene gloves, Nitrile exam style, Utility grade nitrile.

Breakage of tubes containing potentially infectious material in centrifuges not having sealable buckets

- If breakage occurs or is suspected while the machine is running, the motor should be switched off, and the machine left closed (e.g., for 30 min) to allow settling.
- If breakage is discovered after the machine has stopped, the lid should be replaced immediately and left closed (e.g., for 30 min).
- In both instances, the Biosafety Officer should be informed.
- Appropriate gloves should be worn for all subsequent decontamination operations.
- Forceps, or cotton held in the forceps, should be used to retrieve glass debris.
- All broken tubes, glass fragments, buckets, trunnions and the rotor should be placed in a noncorrosive disinfectant known to be active against the organisms concerned.
- Unbroken, capped tubes may be placed in disinfectant in a separate container and recovered.
- The centrifuge bowl should be swabbed with the same disinfectant, at the appropriate dilution, and then swabbed again, washed with water and dried.
- All materials used in the clean-up should be treated as infectious waste and appropriately decontaminated and discarded.

Breakage of tubes inside sealable buckets (safety cups)

- All sealed centrifuge buckets should be loaded and unloaded in a biological safety cabinet. If breakage is suspected within the safety cup, the safety cap should be loosened and the bucket autoclaved.
- Alternatively, the safety cup may be chemically disinfected.

The contact details of authorities to be contacted in case of emergency should be displayed on the facility. The following emergency equipment must be available:

- First-aid kit, including universal and special antidotes
- Appropriate fire extinguishers, fire blankets
- Others, as required:
- Full protective clothing
- Full-face respirators with appropriate chemical and particulate filter canisters
- Room disinfection apparatus, e.g., sprays and formaldehyde vaporizers
- Hazard area demarcation equipment and notices.

3.7.5 Natural Disasters

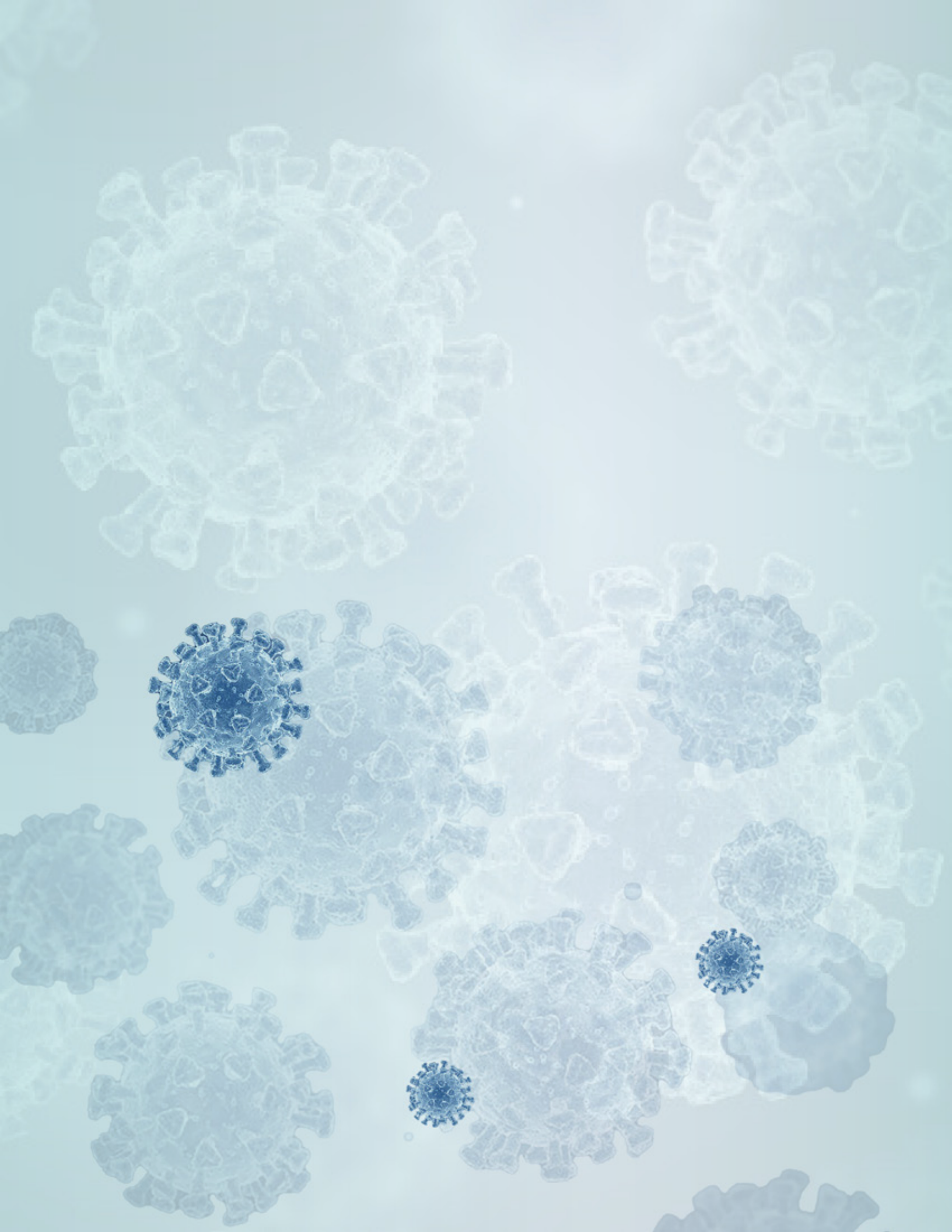
After a natural disaster, local or national emergency services should be warned of the potential hazards within and/or near laboratory buildings. They should enter only when accompanied by a trained laboratory worker. Infectious materials should be collected in leak-proof boxes or strong disposable bags. Salvage or final disposal should be determined by biosafety staff based on local ordinances.

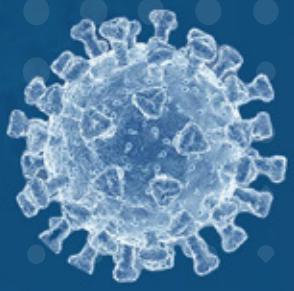
3.7.6 Maintenance

For the sustained use of the BSL-3 Laboratory, it is important that the repairs, servicing and changes/amendments are timely and properly executed and should be periodically monitored. For this, proper maintenance plans and procedures need to be developed. The major maintenance requires re-review of the contingency plan for emergency during regular operation mode so that any possible failure of any ongoing controls such as BMS, UPS, DG set and autoclaves can be handled without breaching biosafety. In case of non-sustainability of emergency, a contingency plan for exit should be evolved. The services of appropriate agency shall be hired, and contract for comprehensive annual operation and comprehensive maintenance services be executed. A Memorandum of understanding should be signed with the contractor and sub-contractors for providing support for at least five years for the spares and services as and when needed.

The comprehensive operation and maintenance services to be provided by the contractor shall include:

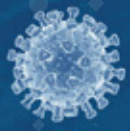
- Providing qualified, experienced and trained manpower for handling operation of the laboratory facility on a day-to-day basis on all working days
- To carry out routine and preventive servicing and maintenance of the equipment, system and services like chiller, AHU, exhaust blowers, autoclave, biosafety cabinet, pass box, access control system, BMS, building electrical system, fire alarm system, etc., installed in the facility.
- Attend to and carry out any breakdown maintenance works required from time to time, as and when it occurs, and be notified by the employer.
- Maintain daily log sheet of laboratory operating parameters
- Providing spares and consumables for various equipment, systems and services like BMS, access control systems, gaskets (for doors and pass box), filters, valves, light fittings, spare switches and sockets, etc. and maintaining suitable inventory at site during the period.
- Maintenance of electrical system, services and construction works executed by the contractor
- Annual Validation of the Laboratory Facility.

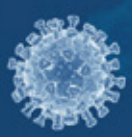




CHAPTER 4

CERTIFICATION OF BIOSAFETY LEVEL 3 (BSL-3) FACILITY





CHAPTER 4 CERTIFICATION OF BIOSAFETY LEVEL 3 (BSL-3) FACILITY

4.1 Certification Mechanism of BSL-3 Facility

BSL-3 lab certification refers to the process by which a laboratory is evaluated and certified to operate at BSL-3 containment level. BSL-3 laboratories are designed for handling and studying potentially dangerous or exotic agents that can cause serious diseases in humans and animals. The certification process for BSL-3 labs in India typically involves a review of several parameters as listed below:

- Facility design and construction: The lab must be designed and built according to specific guidelines, as detailed in the previous chapter, to ensure proper containment of hazardous materials. This must be documented in proper commissioning and validation reports.
- Standard operating procedures (SOPs): The lab must develop, implement and document detailed SOPs for all activities performed within the facility, including handling and disposal of hazardous materials, decontamination procedures, and emergency response protocols.
- Training and competency: All personnel who would be working in BSL-3 lab must receive appropriate training on BSL-3 practices and procedures. This includes training on personal protective equipment (PPE) usage, waste management, emergency response, and understanding the specific risks associated with the agents being handled. This must be documented.
- Documentation: The lab is required to maintain thorough documentation of all procedures, safety protocols, training records, and any incidents or accidents that occur within the facility.
- Biosafety risk assessment: An assessment is conducted to identify potential hazards within the lab and develop appropriate risk mitigation strategies. A biosafety manual must be available. This involves evaluating the agents being handled, the procedures performed, and the lab's containment systems.
- On-site inspection/validation report: An independent regulatory or accrediting body shall conduct an on-site inspection of the lab to verify compliance with BSL-3 standards. This includes evaluating the physical containment infrastructure, reviewing documentation, and observing lab practices.
- Maintenance: Maintenance SOPs, daily monitoring charts and logs of maintenance work must be available.

After validation of the facility and compliance with the requirements as per the guidance described in this document and before initiation of research work, the organization is required to apply for facility certification. With regard to Certification of BSL-3 facility of entities (such as Institutions/ Universities/ S&T organizations/ Educational organizations/ Societies/ Autonomous bodies) falling under or related to the Central Government, the relevant approvals will be dealt with, by the concerned line Ministry of the Government of India.

For Certification of BSL-3 facility of entities falling under or related to the State Government: those pertaining to the Ministry

of Health shall be dealt by DHR, ICMR/ DoH&FW, while Certification of facilities established in other State Government institutions may be undertaken by DBT.

In respect of all other entities, i.e., Non-Governmental Organizations undertaking research and development activities, the Expert Committee constituted by DBT for certification of the BSL-3 facility shall review the application for Certification of BSL-3 facility and recommend them to RCGM, DBT for approval of Certification of BSL-3 facility. This mechanism is applicable to all the existing and new BSL-3 facilities under the entities mentioned above. Certification mechanism for BSL-3 diagnostic labs and manufacturing units shall be issued separately.

The concerned line Ministry of the Government of India may constitute an Expert Committee for Certification of BSL-3 facility, comprising of Subject matter experts, Scientists experienced in establishing/ working in BSL-3 laboratory, Engineers experienced in establishing/installing/ testing/commissioning/maintaining BSL-3 laboratory and representative of CPCB, for reviewing the application for certification and forwarding the recommendations to respective line Ministry. Till the constitution of the Expert Committee for Certification by the respective Line Ministry, certification of BSL-3 facility may be considered by the Expert Committee for Certification of BSL-3 facility, constituted by DBT for the purpose. The Process flow for BSL-3 facility certification is provided below for reference:

PROCESS FLOW FOR BSL-3 FACILITY CERTIFICATION

FOR NEW FACILITIES | **FOR EXISTING FACILITIES**

Facility Design & Establishment, as per Technical/Engineering Standards

↓

Testing (Testing of Equipment/ Critical Components, their functioning to be repeated and demonstrated to the Laboratory In-charge/Biosafety Officer)

↓

Commissioning (Verification of physical construction with predetermined performance criteria and documentation of critical containment components, equipment start-up, adjustments of parameters, control system calibration, balancing and performance testing)

↓

Validation (Represents successful completion of commissioning and acceptance of operational protocols that meet the required design parameters as per Statutory bodies and National biosafety guidelines, conducted by ISO/IEC17025 Accredited Organization)

↓

Application for Certification of BSL-3 facility for **Desk Review**

For **Central government entities,** Application for Certification of BSL-3 facility to be submitted to Concerned line Ministry of Government of India	For **State government entities** pertaining to Ministry of Health, same to be submitted to DHR, ICMR/ DoH&FW; while from other State Government entities to be submitted to RCGM, DBT	For **Non-Governmental Organizations** undertaking research and development activities, application for certification of BSL-3 facility to be submitted to RCGM, DBT

Controlling Line Ministries may constitute **Expert committee for Certification**, including Experts and Engineers experienced in working/establishing/maintaining BSL-3 facility and Representative of CPCB.

Note: *Till constitution of Expert committee by respective Line Ministry, certification of BSL-3 facility may be considered by the Expert Committee for Certification of BSL-3 facility, constituted by RCGM, DBT for the purpose*

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Site/Facility Visit, If Required

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Controlling Line Ministry shall issue **Certificate of compliance for BSL-3 Facility** to the organization seeking BSL-3 certification

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Each Controlling Ministry shall communicate to **RCGM, DBT,** which shall **note the information regarding Certification of BSL-3 facility**

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Certification of BSL-3 Facility, Issued For 3 Years

↓

Annual Revalidation of Essential parameters of Facility, as per Technical Standards

↓

Annual Report of Validation to be submitted to respective Controlling Ministry

Renewal of Certification

Note: If a facility maintains annual validation continuously, then certification will be automatically renewed on expiry of three years. However, if a facility misses two consecutive annual validations, then the facility will have to reapply for certification.

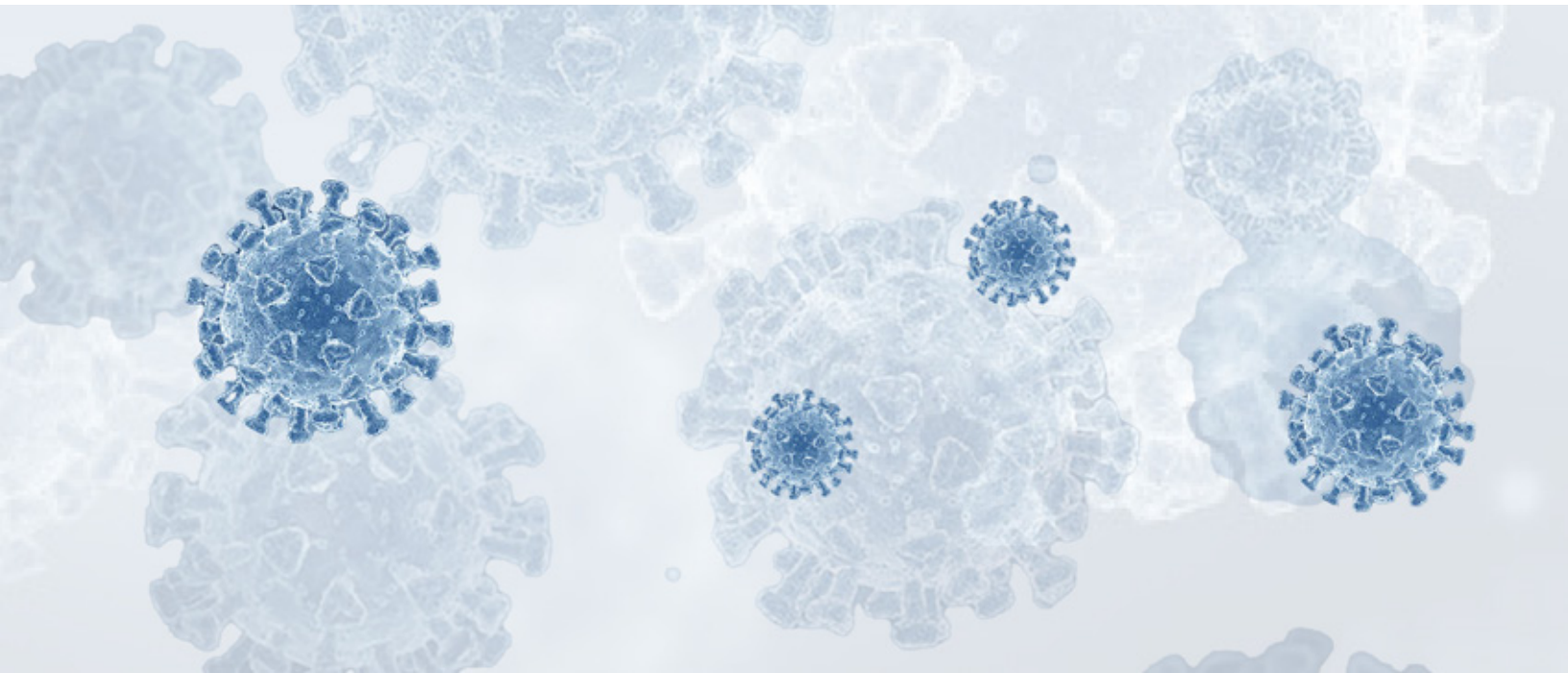
The following are the key steps/processes involved for Certification of BSL-3 labs:

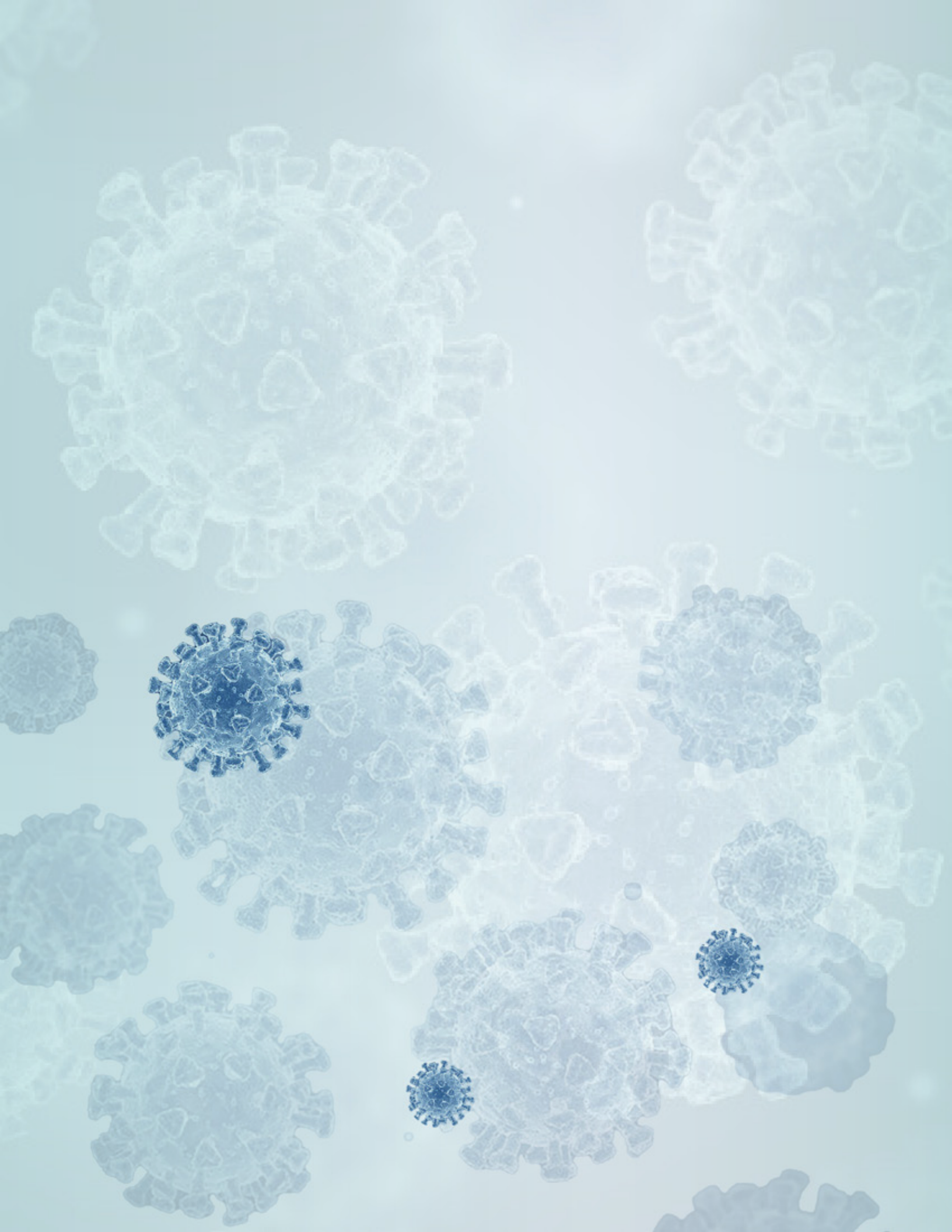
- Each lab needs to submit an application as per ***Annexure VI***.
- Each lab should have conducted a risk assessment and undertaken risk reduction activities. The exercise should be documented and approved by the Institutional Biosafety Committee. This document needs to be shared with the certification committee.
- Further, the IBSC of the organization seeking BSL-3 certification shall submit an undertaking as per ***Annexure VII***.
- The Expert Committee constituted for BSL-3 certification, after review of the application, may recommend and conduct site visits, if required, to ascertain the information provided by the Laboratory In-charge.
- The Controlling line ministry, based on the recommendations of the Expert Committee constituted for Certification, shall issue certificate of compliance for BSL-3 facility. A list of such certified labs shall be communicated to RCGM, DBT for information. A similar certificate will be issued by RCGM, DBT for BSL-3 facilities in Non-Governmental Organizations undertaking research and development activities.
- The certificate for BSL-3 facilities shall be issued for three years, with re-validation of essential parameters on an annual basis.

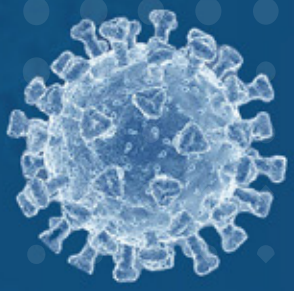
4.2 Annual re-validation

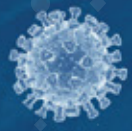
The Certificate for BSL-3 facilities shall be issued for three years, with re-validation of essential parameters of the facility on an annual basis. The facilities must be re-validated and documented at least annually. Therefore, the revalidation of essential parameters of the facility needs to be conducted annually as per technical standards, and an annual report of validation to be submitted for consideration of the respective controlling ministry.

For non-Governmental Organizations undertaking research and development activities, an annual report of validation of essential parameters of the facility needs to be submitted for consideration of the RCGM, DBT. The technical standards for engineering controls for the revalidation of the essential parameters of the BSL-3 facility have been provided in ***Annexure IV***.

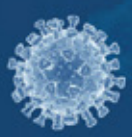








ANNEXURE



ANNEXURE I

KEY STEPS INVOLVED IN RISK ASSESSMENT

Points to be considered during biological risk assessment

- The backbone of the practices of biosafety is risk assessment.
- While there are many tools available to assist in the assessment of risk for a given procedure of experiment, the most important component is professional judgment.
- Risk assessments should be performed by the individuals most familiar with the specific characteristics of the organisms being considered for use, the equipment and procedures to be employed, animal models that may be used, and the containment equipment and facilities available.
- The Laboratory In-charge or Principal Investigator is responsible for ensuring that adequate and timely risk assessments are performed, and for working closely with the institution's biosafety committee and biosafety personnel to ensure that appropriate equipment and facilities are available to support the work being considered.
- Once performed, risk assessments should be reviewed routinely and revised when necessary, taking into consideration the acquisition of new data having a bearing on the degree of risk and other relevant new information from the scientific literature.
- One of the most helpful tools available for performing a microbiological risk assessment is the listing of risk groups for microbiological agents. However, a simple reference to the risk group for a particular agent is insufficient to conduct risk assessment and other relevant new information from the scientific literature must be consulted.
- No one standard approach or correct method exists for conducting a risk assessment.
- However, several strategies are available, such as using a risk prioritization matrix, conducting a job hazard analysis, or listing potential scenarios of problems during a procedure, task or activity.

Risk Prioritization Matrix

The process involves the following five steps:

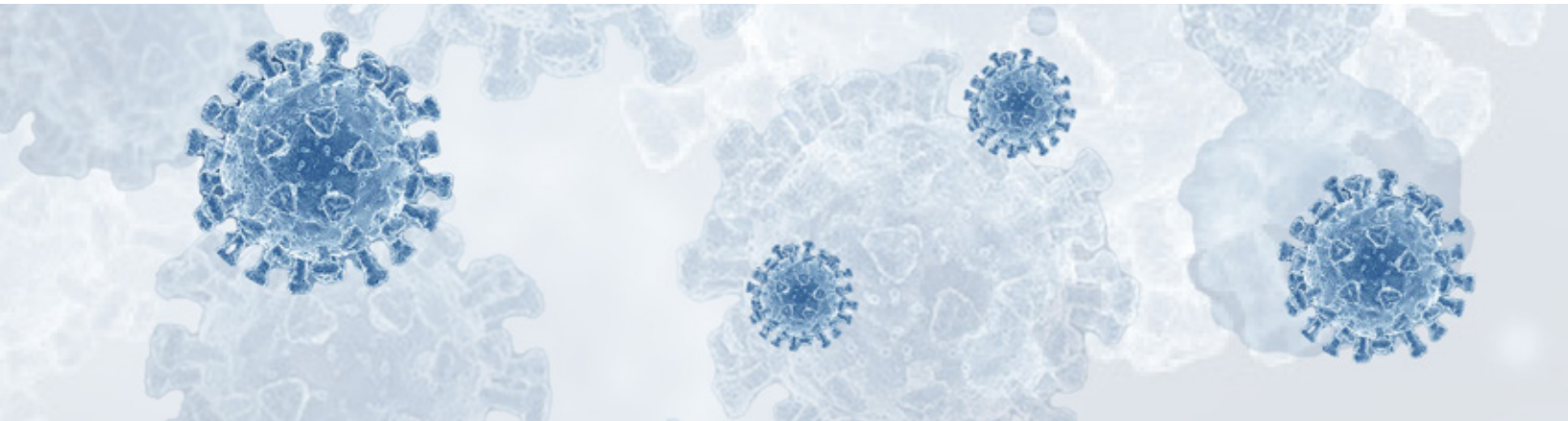
- Identify the hazards associated with an infectious agent or material
- Identify the activities that might cause exposure to the agent or material.
- Consider the competencies and experience of laboratory personnel.
- Evaluate and prioritize risks (evaluate the likelihood that an exposure would cause a laboratory-acquired infection and the severity of consequences if such an infection occurs).
- Develop, implement, and evaluate controls to minimize the risk of exposure.

Likelihood	Consequences				
	Insignificant	Minor	Moderate	Major	Severe
Almost certain	M	H	H	E	E
Likely	M	M	H	H	E
Possible	L	M	M	H	E
Unlikely	L	M	M	M	H
Rare	L	L	M	M	H

L: Likely, M: Medium, H: High, E: Extreme

Other factors that should be considered as appropriate include:

- Pathogenicity of the agent and infectious dose
- Potential outcome of exposure
- Natural route of infection
- Other routes of infection resulting from laboratory manipulations (parenteral, airborne ingestion)
- Stability of the agent in the environment
- Concentration of the agent and volume of concentrated material to be manipulated
- Presence of a suitable host (human or animal)
- Information available from animal studies and reports of laboratory-acquired infection or clinical reports
- Laboratory activity planned (sonication, aerosolization, centrifugation, etc.)
- Any genetic manipulation of the organism that may extend the host range of the agent or alter the agent's sensitivity to known, effective treatment regimens
- Local availability of effective prophylaxis or therapeutic interventions.
- Based on the information ascertained during the risk assessment, a biosafety level can be assigned to the planned work, appropriate personal protective equipment selected, and Standard Operating Procedures (SOPs) incorporating other safety interventions developed to ensure the safest possible conduct of the work.
- Each laboratory should adopt a safety or operations manual that identifies known and potential hazards, and specifies practices and procedures to eliminate or minimize such hazards.



ANNEXURE II

TECHNICAL STANDARDS FOR THE ENGINEERING CONTROLS FOR BSL-3 LABORATORY

The technical standards which a BSL-3 laboratory must abide by are listed below:

S. No.	PARTICULARS
I	FACILITY FEATURE
1	Access Control: Due to the biosafety and biosecurity concerns over the usage of biohazardous materials, access to the biocontainment facility must be strictly limited to trained and authorized personnel only. The access to the laboratory must be controlled electronically that could be ensured through access card, biometric, or PIN security access. Access Control System having USB port for communication and data back-up should be available in the BSL-3 facility. There should be provision for door interlock system with electro-magnetic locks and control panel.
2	Personnel Entry/Exit in lab through Clothing Change & Shower Rooms: Shower doors located between the clean and dirty change room should not to be opened simultaneously. These doors should be interlocked electronically and /or mechanically. Additionally visual and audible alarms are recommended. There should be manual override facility to interlocking in case of emergency. Facility should preferably have separate entry/ exit for Ladies and Gents wherever appropriate.
3	Materials, Supplies & Equipment should enter/ leave through Double Door Autoclave, fumigation chamber / Airlock with inter locked doors. Doors should be interlocked electronically and /or mechanically. Additionally, visual and audible alarms are recommended.
4	Work Conducted in Primary Containment Equipment: Work should be conducted in a Biosafety cabinet. The BSC may be selected based on protection assessment, work assessment, Chemical vapour generation assessment. In general, BSC Class II is recommended.
5	Hand Washing station: Should be placed near the laboratory exit. Provision for sensor-based or foot / elbow operated eye wash station should also be there.
6	Laboratory and animal room wastes from the containment area to be decontaminated or sterilized before disposal. A Double door barrier autoclave with interlocking of doors and other controls. Waste material is loaded in the autoclave from the facility and removed from outside the facility after autoclave selected cycle is completed.
7	Lab clothing: Lab clothing should be decontaminated by autoclaving before washing.

8	Animal cages: may be autoclaved or thoroughly decontaminated by cleaning with hot water at 82 °C.
9	Appropriate cautionary signs: Appropriate hazard signs should be pasted for BSL-3 on the main entrance door of the laboratory.
10	The facility should be located in a separate building or isolated zone within a building as per “Box-in-Box” principle, i.e., more containment area is surrounded by less containment area. If the infectious work is handled in the primary barrier such as BSCs and IVCs the lab room acts as secondary barrier.
11	Pass through cabinets /dunk tanks for transfer of biological materials. Door interlocking with override facility. Dunk tank, as feasible, based on risk assessment.
12a	Steam Glassware sterilizer: Single door/ double door based on requirement.
12b	Ethylene Oxide barrier autoclave or fumigation airlock should be used for materials which cannot be steam autoclaved.
13	Liquid Effluent (Bio-Waste) Treatment should be conducted based on risk assessment.
14	Personnel change room is recommended for laboratory work.
15	Shower: the availability of shower within facility at the exit is recommended for a BSL-3 laboratory work but is mandatory for high-risk work. Drain water from such shower cannot & should not be disposed of in municipal waste without treatment. It must be ensured that such water flows down to designated drain for treatment and must not remain stagnant on floor.
16	Lab contiguous with shower: These showers are in addition to shower at the exit of the facility and are required in animal houses and high-risk areas. Drain water from such shower must be treated in effluent treatment system before disposing in municipal waste.
17	Work surfaces: bench tops impervious to water, resistant to acids, alkalis, organic solvents and moderate heat and should be monolithic.
18	Interior surfaces of walls, floors and ceilings: monolithic, resistant to liquids and chemicals, all penetrations to be sealed. All floor drains should have adequate water seal traps filled with chemical disinfectant (chemical would need frequent topping up). Epoxy resin is recommended for flooring. Epoxy, PU, low-lustre acrylic or latex enamel paint is recommended for walls. Wall and floor junction should be coved to walls and sealed.
19	All Windows should be fixed type and sealed windows should be made with unbreakable double glass.
20	Vacuum outlets (if provided) should be protected by HEPA filters & liquid disinfectant in traps. HEPA filters (with efficiency of 99.97% or better) must be validated annually or replaced annually.
21	Other liquid & gas services protected by backflow preventers, as per services required in lab.
22	Sewer and other vent lines should be appropriately protected.
23	Ventilation Facility: independent supply & exhaust air systems.
a	Air tight leak proof duct (Tested for leakages): Required

b	Single Pass / once through system (No Recirculation): Required
c	Directional Air Flow: Required
d	Pressure Gradient: Required
e	Supply/ exhaust fans interlocking: supply fan to start only after exhaust fan is switched on
f	Ventilation Containment Equipment: Class II or Class III BSC depending on risk assessment.
24	Direct Digital Control (DDC) and Building Automation System (BAS) are required
25	Leak tightness testing & validation of critical components of the biological containment system prior to final acceptance of the completed work is required, as per national guidelines. Duct work should be tested by pressure decay method (as provided at ***Annexure III***).
II	**ARCHITECTURAL CONSIDERATIONS**
26	Laboratory Layout: In general, columns and beams inside the lab may be avoided if possible.
a	The designing of a biocontainment laboratory must consider laboratory personnel, material, pathogen flow routes; activities to be carried out; and facilities including laboratory equipment required in the containment laboratory. The engineering services required for the laboratory as well as equipments in the laboratory need to be identified so that provision can be kept for the services while designing the lab.
b	BSL-3 laboratory design should be rodent and insect-free.
c	Adequate means of outlets shall be provided from laboratories without breaching containment or leading to cross-contamination. Airlocks shall be provided at transitional points between the spaces of different biocontainment levels through which personnel and/or material must pass.
d	The entry/exit should be through cloth change and additionally, through shower room while exiting. The need and number of showers shall be as per the laboratory SOP and requirement.
e	For equipment and other material which cannot be autoclaved, the facility should have Airlock with gaseous decontamination system and interlocking of doors so that only one door opens at a time. Once a dirty side door is opened, the clean side door should open only after decontamination cycle is completed. If formaldehyde is used for gaseous decontamination, then it should be neutralised by ammonia. SOPs must be developed by the Laboratory In-charge.
f	Facility must have an emergency exit in case of fire or other emergency and must have an override facility with interlocking of all exit doors. Facility-specific SOPs may be developed for exit from the facility, in case of emergency. Maintenance of the emergency exit door may be done at regular intervals as developed for preventive maintenance. Emergency door should remain closed and its key should be kept in a glass box nearby.

g	The emergency door must only be opened in the event of an emergency or at the time of mock drill. SOPs for opening of emergency door should be developed by the Laboratory In-charge and tested with frequency at least once in a year,
h	For large facilities, if washrooms are required, then effluent from the washroom should also be decontaminated before disposing of in the municipal sewer system. To prevent reverse airflow from the drain lines, it is essential to choose appropriate drain traps to withstand maximum negative pressure as per the risk assessment. A suitable example could be that washroom drains should have a minimum 125mm trap and it should be ensured that the trap is always filled with water for sealing and sewer line should be appropriately protected.
27	Room Envelope and Interior Finish
a	The design should include construction materials and finishes that are compatible with respective research activities and decontamination methods. Floor should be made of epoxy material and seamless, impervious, abrasion resistant, non-slip when wet and cleanable. The floor should be able to withstand disinfectants and be washable with 82 °C hot-water containing detergents and the decontamination liquids under hose pressure. Walls of the labs must be constructed with non-porous materials with industrial grade epoxy paint.
b	Doors, frames, casework and bench tops should be non-absorptive; the use of organic materials should be avoided.
c	Surfaces to be scratch, stain, moisture, chemical and heat resistant in accordance with laboratory function. Surfaces to provide impact resistance in accordance with laboratory function. Surfaces to be continuous and compatible with adjacent and overlapping materials (i.e., to maintain adhesion and a continuous perimeter); wall and floor welded seams are acceptable in BSL-3 laboratories.
d	Continuity of seal to be maintained between the floor and wall (a continuous cove floor finishes up the wall is recommended).
e	Interior surfaces to minimize movement of gases and liquid through perimeter membrane. Interior coatings should be gas and chemical-resistant in accordance with laboratory function (should be able to withstand chemical disinfection and fumigation). Interior coatings should be cleanable.
f	Bench tops should not have open seams. Bench tops should contain spillage of materials (e.g., with marine edges and drip stops). Benches, doors, drawers, door handles, etc. should have rounded rims and corners.
g	Backsplashes, if installed, should be tight placed along with wall and sealed at wall-bench junction.
h	Reagent shelving should be equipped with lip edges.
i	Cabinet doors must be self-closing and lockable. Drawers should be of one-piece construction and equipped with catches.

28	Heating Ventilation and Air Conditioning (HVAC)
a	For isolation, separate air handling systems should be installed in non-containment and containment zones. Further, AHUs should be installed in each isolation zone, wherever isolation is required within the containment area. Each air-handling unit serving a containment area shall supply 100% fresh air. Wherever feasible and economical, heat recovery may be done from lab exhaust air.
b	Direction of air flow should be from less contaminated area to more contaminated area. Air flow within containment area should be from entrance to rear area. All laboratory rooms must be provided with a visual monitoring device that indicates directional inward air-flow.
c	There should be 8-12 air-changes per hour for laboratory and 10-12 for ABSL-3.
d	Differential pressure of a minimum of 15 Pascal should be maintained between separate functional spaces to ensure more negative pressure in those areas which are at higher risk of contamination. The BSL-3 facility is recommended to be maintained at differential negative pressure of 15, 30 and 45 Pa. All negative pressure in the containment area should be measured with reference to common single atmospheric set point.
e	HVAC system must be capable of sensing and responding to unusual outside pressure conditions (like a storm) and maintaining negative pressure in the containment area during all weather conditions. For the ease of maintenance, active components of HVAC system must be kept outside containment area with provision for sufficient space for maintenance of components. The capacity of exhaust system must be approximately 15% more than the supply air system. Variable speed drive on the exhaust fan is recommended to facilitate room pressure control adjustments. HVAC system must be controlled by electronic control system or BAS.
f	Air duct for supply and exhaust should be air tight up to zero leakage dampers. Isolation valves should be provided in HEPA Filter housing to avoid any leakage of contaminated air and for provision of gaseous decontamination of laboratory, in case of breakdown of AHU. Duct should be tested for any leakage before commissioning of laboratory by soap bubble test or pressure decay test at +1000 Pascal pressure. Ducting should be of SS-304 material to avoid rusting of duct work.
g	Structural stability to withstand 1.25 times maximum design pressure under supply and exhaust fan failure conditions (no wall distortion or damage should occur).

h	The exhaust air from all the containment equipment and containment area shall be filtered through HEPA/ULPA filters before discharging outside. Efficiency of HEPA/ULPA filters should be better than 99.97%. HEPA/ULPA filter housing shall have provision of Isolation valves on both upstream and downstream sides for decontamination of HEPA/ULPA filters during maintenance. HEPA filter housing should have pressure differential meter to know the status of any choking of filters.
i	Pre-filters shall be installed in upstream side of HEPA filters to increase the life of HEPA filters in both supply air and exhaust air. Exhaust pre filters can also be installed within the containment area where they can be changed easily. Used pre-filters should be decontaminated before removal from the containment area.
j	HEPA filter housing should have in-situ leak testing facility to assure integrity and damage in installation of HEPA filter and leakage testing of HEPA filter sealing with its housing. Supply and exhaust HEPA filter housings should be located as close as possible to the containment space to reduce the containment duct length. HEPA filter housing should have provision for physical isolation using zero leakage bio seal dampers. Housing should also have provision of port for injecting chemicals for decontamination of HEPA filters before their removal for replacement. For existing facilities which do not have above provision, they should develop SOP for safe maintenance and HEPA filter replacement. Bag-In-Bag-Out (BIBO) HEPA filters may be preferred or HEPA filter housings may be kept under negative pressure.
k	In areas with higher contamination, double HEPA filters in series are recommended. HEPA filters may be required to be installed in parallel depending upon the quantity of air to be filtered based on containment area. HEPA filters may be designed for approximately 50% of their rated capacity so that there is sufficient margin for dust loading as capacity of filter reduces with the choking of HEPA filters.
l	To ensure that, there is no mixing of exhaust and supply air, exhaust should be discharged at a safe distance from the supply air. A suggestive distance between supply and exhaust to achieve this could be 7 m. Exhaust air should be discharged in such a direction that it has minimum impact on storm/wind direction. Air from the containment space is to be discharged preferably from the roof and in vertically upward direction at a velocity to maintain the desired negative pressure in all the containment areas. HVAC system must be capable of discharging air at a velocity greater than 3000 fpm (900 meters per minute) to maintain negative pressure in the containment area during unusual outside pressure in worst weather conditions like storm etc. The exhaust should be suitably designed to prevent rainwater entry.

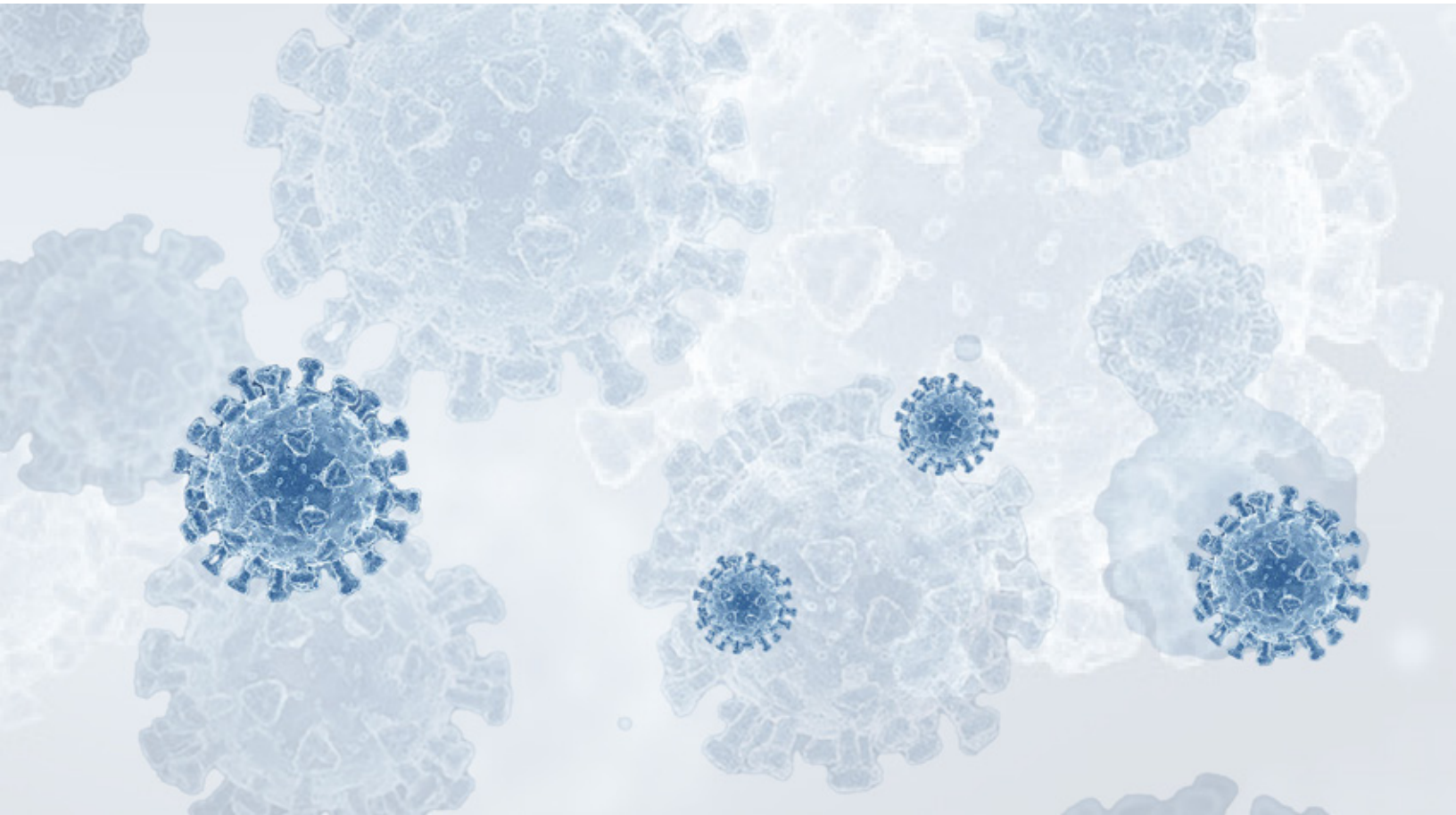
m	Outside air intake should be such that rain should not wet or clog the supply air filters. Air intake may be protected with 6 mm or 12 mm bird screen.
n	As a general principle, design must ensure that failure of electrical, mechanical or power sources will not shut down critical biocontainment systems. Therefore, sufficient redundancy should be kept based on risk analysis based on criticality and cost factors. Standby fans and pumps should be considered in supply and exhaust air ventilation systems. To prevent overheating of interior rooms, N+1 number of chillers should be considered (N being the number of best size chiller).
III	**MECHANICAL**
29	Air compressor, if required for pneumatic controls and for compressed air supply in the BSL-3, should be oil- and moisture- free, and installed outside the containment area. Sound level should be less than 60 DB and must be installed on vibration isolators. Air compressor must have moisture separator with automatic moisture drain valve.
30	Analysis may be done to have a centralized steam generator (oil-fired boiler) or electric boiler, or stand-alone electric steam generators depending on requirement. Steam is required for autoclave, liquid waste decontamination and hot water generator for central heating/personnel showers etc.
31	BSL-3 facility must have DG generator for 100% load requirement with AMF panel. Fuel storage capacity should be designed keeping in view local load shedding and continuous run of generator for long time due to electric supply break down. DG set should be housed in environment friendly enclosure and must meet CPCB norms. Noise level should be less than 60 DB. Standby generator is recommended. However, its cost and risk analysis may be done at the design stage.
IV	**SERVICES**
32	Service pipes shall be installed with slopping lines. Backflow preventers may be used to isolate branch water lines. For cleaning purpose and to avoid contamination, piping should be mounted at some gap from the wall.
33	Compressed air for instrument control and other requirements should be oil and moisture free, and must have small inline HEPA filters and backflow preventers.
34	Each floor drain should have minimum 125 mm deep trap, which should be directly connected to the effluent treatment plant. It must have cleanout plugs within the containment zone. Liquid waste pipe should be acid and chemical resistant, and leakproof. Drain pipe should be easily cleanable and preferably 150 mm in size.
35	A foot, elbow or automatic operated hand washing station should be provided near the exit of each functional space. Sink should be acid and chemical resistant, preferably of SS or epoxy coated resins.
V	**ELECTRICALS**
36	Separate power and lighting panels should be provided for containment and non-containment spaces. All main distribution panels should be located outside containment space for ease of maintenance.

37	All the inside and outside openings of the conduit, running from non-containment area to the containment area and across different containment areas having differential negative pressure, should be sealed to prevent circulation of air.
38	Sealing should be done at accessible space for inspection and maintenance.
39	All lights should be energy efficient, as per Energy Conservation Building Code (ECBC).
40	Lighting should be in the range of 300 - 500 lux in the laboratory and 700-800 lux in cleaning cycle area.
41	All signage, emergency lights, BAS, communication network, exhaust system to maintain negative pressure and other critical equipment should be provided with online UPS with minimum half an hour backup. There should be a standby UPS of 100% capacity of designed capacity UPS. The capacity of UPS shall be designed based on emergency load of the facility.
42	A standby generator with AMF panel capable of bearing 100% load of the facility should be available in case of power failure.
43	Electrical load should be divided equally in each phase.
44	There should be a centralized voltage regulator to supply +/- 10 % of rated electric supply. Voltage regulator shall be kept outside the facility.
45	Equipments which need servo voltage (+/- 2%) supply may be identified well in advance and central servo stabilizer may be kept outside the facility.
46	Separate cable with 100% capacity of load should be kept as stand-by and shall be used in case of any fault in the main cable to reduce downtime.
47	Electrical load may be properly calculated during the design stage, by keeping in mind, any future addition of equipment(s).
48	Wiring for interlocking of double door entry, airlocks, pass boxes and double door autoclaves should be well planned so that both the doors cannot be opened simultaneously.
49	The electrical system must have sufficient circuits and power to support decontamination need of the facility.
50	Earthing with copper earth plate 600 mm X 600 mm, 3 mm thick along with masonry enclosure and cover plate having 2.7 meter long watering pipe fitted with funnel for watering. Earthing should be separate for neutral and other for earthing as per Indian Electricity Rules. There should be separate similar earthing for electric supply and each generator. Voltage difference between neutral and earth should be less than 5V.
VI	**COMMUNICATION NETWORKS**
51	The laboratory should be equipped with communication network between containment area, outside support area and service areas. The Laboratory areas, support area and service area shall be provided with Data and Voice points for communication. The system shall be complete with required conduit and wiring. The Data and Voice points can be fully wired with CAT5/6 cable or equivalent complete with output terminals. A suitable EPABX system shall be provided for required incoming and outgoing lines, as per the requirement. A system must be connected to a location that has personnel available for emergency response at all times when work is being performed in a BSL-3 laboratory.

52	Fax, LAN network should be provided for electronic transfer of information and data within the containment laboratory as well as from containment laboratory area to outside area. Electronic transfer of information and data should be encouraged, while avoiding paper transfer. However, in case paper has to be taken out from containment area to non-containment area, it must be de-contaminated through autoclave/ fumigation chamber/Air-lock.
53	Security & CCTV installations: It is recommended to install CCTV at Entry, Exit and Containment areas. CCTV System, complete with wall/ceiling mounted high- resolution color cameras, multiplexer cum DVR, LED color monitor, associated power and control cabling along with required hardware and software, shall be provided. In addition to the laboratory area, the video surveillance shall monitor activity outside of the secured space including hallway entrance. Video surveillance cameras should be installed to provide live and recorded video activity inside the laboratory as well as outside of the secured space, in interior activity spaces, and covering materials of interest. The access control and video surveillance system devices should be coordinated to allow for recording and monitoring of entry and exit events. Due to the sensitivity of research, the physical security systems should be integrated to provide for real-time monitoring and auditing of the video surveillance and electronic access control systems. All activities related to movement of laboratory personnel and material should be duly recorded and documented. It is advisable to install a mirror display in Laboratory In-charge's room.
VII	**CONTAINMENT PERIMETERS**
54	A double-door barrier autoclave with bio seal should be located on the containment barrier. Body of autoclave should be located outside of containment for ease of maintenance. Outside room (Clean side) of autoclave should be well-ventilated.
55	Autoclave condensate from autoclave chamber should be directly connected to drain piping system and should be decontaminated along with liquid effluent in Effluent Treatment Plant (ETP). However, condensate from jacket can be recirculated through boiler.
56	Barrier autoclave and pass boxes should be equipped with interlocking door (electrically and /or mechanically) and visual or audible alarms to prevent opening of both doors simultaneously.
57	Autoclave should be PLC controlled and should record complete cycle real-time data like temperature, steam pressure, type of cycle etc. A record of all autoclave cycles should be maintained.
58	Clean side door of barrier autoclave/ fumigation airlock should open only after completion of the decontamination cycle.
59	For materials that cannot be autoclaved (e.g., heat sensitive equipment, samples, films etc.), other proven technologies for material decontamination (e.g., chemical, gaseous) should be provided at the barrier. SOPs to be developed by the Laboratory In-charge.
60	Dunk tank and double door pass box with gaseous decontamination with interlocking of doors should be available at the barrier of the facility.
61	All penetrations should be sealed with non-shrinkable sealant and tested for leakage at the time of testing and commissioning.

62	Containment side of barrier autoclave, Necropsy room (Post-mortem room) and effluent treatment room are highly contaminated areas. Hence, negative pressure of these areas should be accordingly kept at more negative value.
63	All extended part of utilities such as ducting, drain lines etc this extended part needs proper protection from external hazards.
VIII	**DECONTAMINATION**
64	For personnel, change of laboratory clothing in change room and shower is recommended.
65	Air exit should occur only after HEPA filtration.
66	Liquid waste is decontaminated by steam liquid effluent treatment or by dosing chemical disinfectant.
67	Solid wastes should be taken out of the facility through steam autoclave.
68	Equipment which cannot be autoclaved should be taken out after gaseous decontamination.
IX	**BUILDING MANAGEMENT SYSTEM**
69	A customized building management system shall be designed, programmed and provided to manage the facility through monitoring and controlling the operation of critical equipment like HVAC system and other laboratory operating parameters like: Room/Area/ zone pressure, Room/Area/zone temperature & RH, Ambient temperature & RH, AHU and Exhaust Blower operating status, Variable Frequency Drive (VFD) status & Variable Air Volume (VAV) status, OPEN/Close dampers status, and Supply & exhaust air quantity in each BSL-3 Laboratory rooms/zone. The supply and exhaust air duct of each BSL-3 Lab Rooms/Area shall be provided with VAV device with flow measurement sensor for adjustment and balancing of the desired supply and exhaust air quantities. The Air Handling Units and Exhaust Blowers shall be provided with VFDs. The VAVs and VFDs shall be controlled to maintain the set laboratory inside pressure conditions through BMS Program. The Building Management System shall allow Start/Stop operation of the Complete HVAC system in Auto Mode. However, the system shall have the provision to override the parameters (password protected) and to enable START/STOP operation of the HVAC system in Manual mode, as well. The BMS shall provide alarm in case of HVAC system failure, collapse in room/zone negative pressure and deviation of any operating parameter from the set limits. Each BSL-3 Laboratory Rooms/Zones area shall be provided with Pressure Sensors, Temperature Sensors and RH Sensors, wired and integrated with the BMS to display the operating conditions. The Building Management System shall be complete with PLC, Sensors, Controllers, power and control wiring, customized Software and other associated field devices, hardware and accessories complete in all respects, as per requirement and approved design. The HVAC system Start and Stop sequence shall be interlocked to prevent positive pressurization of the BSL-3 laboratory, at any point of time. A dedicated desktop PC shall be provided for the BMS operation and control along with a parallel secondary display screen at the BSL-3 laboratory entrance to show the operating parameters. The BMS control panel shall be powered through UPS. Upon restoration of power after a power failure, the BMS shall start the HVAC system automatically without any human interface and restore the normal operational set points of the system. It is advisable to install a mirror display in Laboratory In-charge's room.

X	FIRE DETECTION AND ALARM SYSTEM
70	The BSL-3 Laboratory and support areas shall be provided with fire detection and monitoring system with alarm facility along with provision for manual fire extinguishers. The Fire hazard must be notified through both local audible and visual alarms. Further, the fire alarm should be differentiated from other alarms (in the BMS), for easy identification and rapid response. The Fire Detection & Alarm System shall be complete with Smoke detectors, Heat detectors, Fire Alarm Panel, manual call points, response indicators, power and control wiring and cabling etc. complete in all respects. Fire Dampers provided in the supply and exhaust air systems shall be interlocked with the AHU blower motors such that in case of fire, the AHU fan motor should trip automatically. Volume Control Dampers, Fire dampers and air diverting vanes shall be provided in the supply and exhaust air ducting, as per the requirements and approved design.



ANNEXURE III

ESSENTIAL TESTS DURING COMMISSIONING OF BSL-3 LABORATORY

Leak testing of supply and exhaust ductwork and Isolation Valves (pressure decay method):

- Leak testing of supply and exhaust ductwork and Isolation Valves (pressure decay method):
- Leak test should be conducted in all the duct portions that are potentially exposed to contamination, i.e., from respective containment rooms to isolation valves.
- All welds and duct joints shall be fully exposed and accessible for inspection and repair until testing is completed and validated.
- Duct and plenums should be isolated by closing isolation valves, which shall be pressurized to 1000 Pa. All the joints need to be physically inspected for any leakage.
- If any leakage is found, it needs to be repaired and again pressurized to 1000 Pa.
- Leakage can be tested by soap bubble test or pressure decay method.

Acceptance:

- No leakage assessed by soap bubble test in duct is acceptable.
- Alternatively, duct work may be tested by pressure decay method.
- Pressure drop less than 0.1% duct volume /min is acceptable.

Factory testing of HEPA filter Housings, Isolation valves, Air tight gates and other critical components:

- HEPA filter Housing, Isolation valves, Air-tight gates and other critical components should have been tested at the manufacturing unit, and QA certificate should be provided.

Acceptance:

- Pressure drop less than 0.1% duct volume /min is acceptable.

Factory testing of HEPA filters:

- HEPA filters should have been tested at the manufacturing unit and QA certificate should be provided.
- Filter media test report of HEPA filter is required.

Acceptance:

- HEPA filters having leakage of less than 0.03% down to 0.3 micron particles are acceptable.
- Efficiency should be 99.97% for 0.3 micron particles.

Field testing of HEPA filters and HEPA filter housings after installation at site:

- Integrity of HEPA filter and Filter housings should be tested in situ by Soap bubble test and Pressure decay method.
- HEPA Filters may be tested after installation by pressure decay method as described above.
- Any pinhole leakage found during scanning is repaired and scanned again.

Acceptance:

- No leakage in filter housing is acceptable.
- Alternatively, integrated filter housing may be tested by pressure decay method.
- Pressure drop less than 0.1% duct volume /min is acceptable.
- HEPA filter having leakage less than 0.01% down to 0.3 micrometre particles is acceptable.

Leak testing of containment spaces:

The purpose of testing the containment space is to determine and minimize the leakage through walls, floors, ceilings, penetrations for service pipes, ducts, electrical conduits and other containment barriers of containment space like autoclave, Pass box, etc. Leakage can be tested by soap bubble test or pressure decay method. Testing is usually done by pressuring positive pressure by approximately 125 Pa and monitoring the air pressure during the test period, using the following method:

- Sealing the supply and exhaust openings, closing all doors and other openings in the containment perimeter.
- Installing inclined manometer/ pressure differential meter of minimum 0-1000 Pa scale and 10 Pa least count.
- Pressuring positive pressure to 125 Pa.
- Visual inspection of possible leakage spaces.
- Soap bubble testing.
- Repairing any leakage observed.
- Repeating the test with 250 Pa.
- Monitoring pressure decay test for 20 minutes.
- Record pressure differential after every minute.
- Release the pressure slowly after the completion of monitoring period.

Acceptance:

- Pressure drop less than 125 Pa (Half of the original 250 Pa) in 20 minutes, is acceptable.

Differential pressures and/ or directional air flows between adjacent areas as per design parameters:

- Differential pressure meters/pressure manometers installed at predetermined spaces are monitored, and readings are recorded while doors are operated as per SOPs.
- Negative pressures of different pressure zones should not equalize during the normal operation of doors.
- Directional airflow is tested with the visual inspection of smoke patterns, while testing is conducted with the help of a smoke generating pencil.

Acceptance:

- Unidirectional smoke patterns from areas of low contamination to high contamination is acceptable.

Field testing of Biological Safety Cabinets:

Standard tests for BSC are classified into two groups:

Critical performance tests that are required to confirm that the cabinet is functioning properly include:

- HEPA filter Installation integrity test.
- Work zone integrity test.

- Biosafety cabinet integrity test.
- Downflow velocity test.
- Face (Inflow) velocity test.
- Air flow smoke pattern test
- Supply and Exhaust Fan interlocking control test.
- Alarm operational check

Non-critical tests which relate to operator's safety include:

- Vibration
- Sound level
- Lighting
- UV light.

Acceptance:

- The result of biosafety cabinet installation, as per NSF/ ANSI 49 standards, is acceptable.

Testing of Air-lock:

- Airlock doors should be tested for leakage by Soap bubble test and Pressure decay test as detailed above.
- Once dirty side door of airlock is opened, airlock gets contaminated; therefore, outer side door/ clean side door should only be opened after air lock has been decontaminated.
- Formalin fumigation is one of the methods recommended for gaseous decontamination.
- Testing of airlock should be done as per SOPs adopted for the lab.

Acceptance:

- The working of airlock decontamination system, as per SOPs adopted, is acceptable.

Testing of steam autoclaves:

Steam autoclaves are tested depending on the number of programs available in the Programmable Logic Controller (PLC), which shall be used in the facility. The effectiveness of decontamination depends on loading factors, material being decontaminated that influence the temperature to which material is subjected and the contact time. Packaging, size of container and their placement in autoclave must allow steam penetration and must be arranged so that steam circulation in the autoclave is free. Some important decontamination programs are meant for/ directed towards:

- liquids
- liquids with pre-vacuum.
- nonporous solid materials
- nonporous solid materials with vacuum.
- fabric material with pre and post vacuum.

It should be ensured that gauges and thermocouples are calibrated. Depending upon the temperature, the exposure period varies from material to material. For testing of effective sterilization, chemical indicators can be used. However, Biological indicators are preferred, as they are the only process indicators that directly monitor the lethality of a given sterilization process.

Note: Chamber temperature should always be more than 121 or 134 °C as per the case. During testing, if the chamber temperature comes down from 121°C or from the set temperature, then time counter should be reset to zero.

Acceptance:

- Appropriate working of chemical/ biological indicators is acceptable.

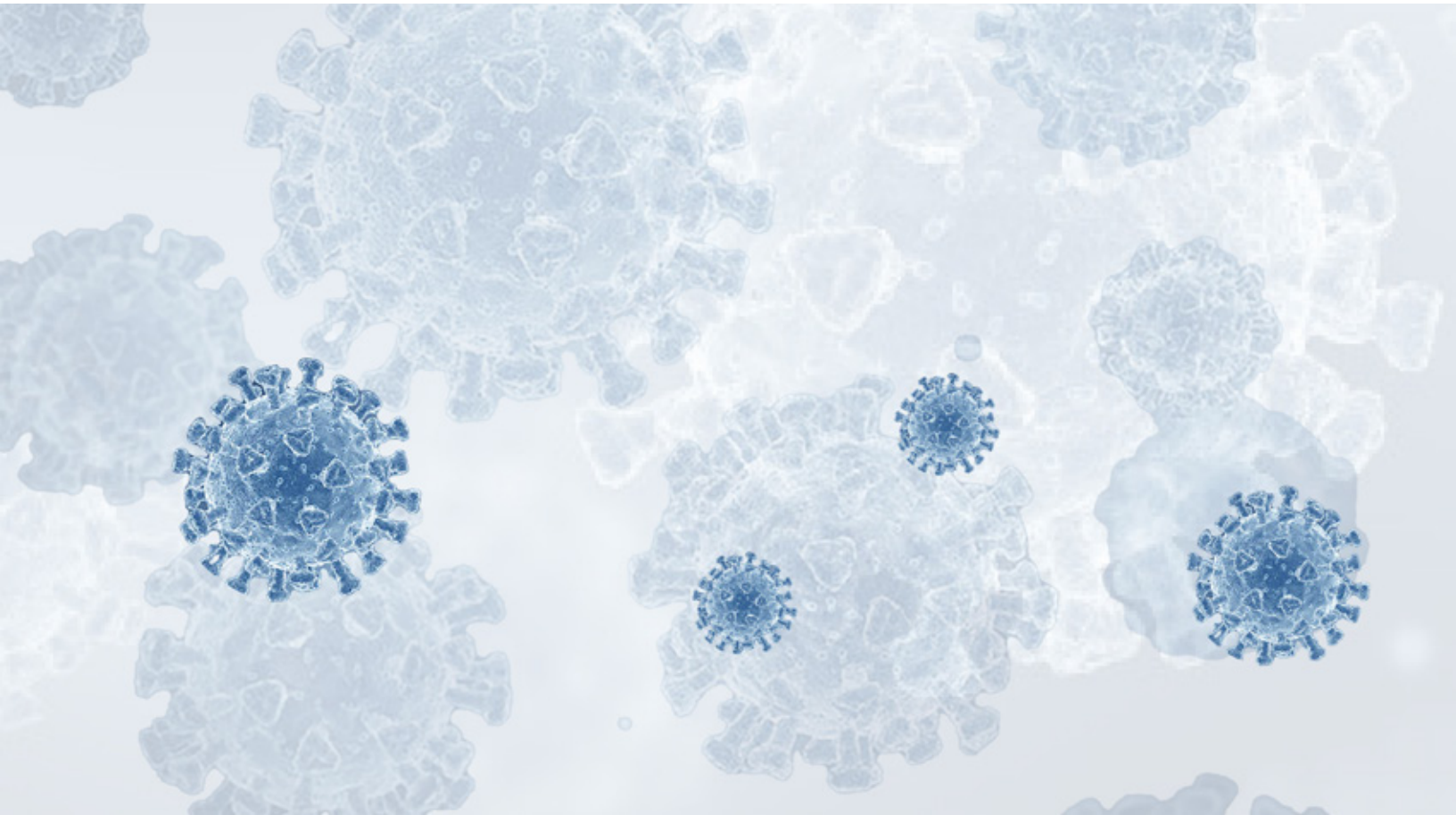
Testing of Interlocking of airlock doors, pass box doors, entry- exit doors, autoclave doors, etc.:

- Interlocking of dirty side door and clean side door is tested as per SOPs adopted

for the lab. Both side doors should not be opened at the same time. Once the dirty side door is opened in air lock/ pass box/ autoclave, then the clean side door should open only after the chamber has been decontaminated as per the SOPs adopted in the lab. In case of entry-exit doors, once the dirty side door is opened then the clean side door should open only after dirty side door has been closed and shower has been taken (it is also recommended that dirty side door should open after one air change of the shower room).

Acceptance:

- The working of interlocking of doors as per the SOPs adopted is acceptable.



ANNEXURE IV

VALIDATION PROCEDURE FOR BSL-3 LABORATORY

Administrative validation to facilitate Operation and Maintenance to ensure the safety of Occupants, Products and Environment:

1 Review background materials that affect maintenance operations:

- Obtain and review Commissioning Report.
- Review architectural and mechanical drawings to ensure facility construction is as per design.
- Review biosafety policies and procedures (SOPs) for the laboratory (facility), including training of laboratory staff and maintenance staff.
- Review hazardous (infectious) waste decontamination procedures.
- Assess the laboratory accident response protocols.
- Review integrated pest management program.
- Review SOPs for document retention, maintenance and lab procedures.

2 Inspect and Evaluate:

Finishes, penetrations & caulking integrity for architectural elements such as doors, around the ceilings, lighting fixtures, electrical devices, etc., within containment to meet requirements for:

- Clean-ability of all surfaces, including furniture
- Smoothness of all surfaces
- Sealed seams and penetrations
- Monolithic, slip-resistant floors
- Surface impermeability to liquids
- Resistance of surfaces to chemicals (organic solvents, acids, alkalis), disinfectants and moderate heat
- Gas tightness for decontamination
- Pest management requirements
- Non-openable bio-seal windows.

3 Inspect room layout, placement of equipment and equipment condition:

- Evaluate autoclave verification testing procedures, inspect log book
- Evaluate access control and exit procedures
- Evaluate the availability of:
  a. Emergency equipment
  b. Emergency two-way communication system
  c. System provided for electronic transfer of information to outside of containment area.
  d. Emergency lighting
  e. Availability and Working fire extinguishers
  f. Availability of chemical spill kit within containment
- Evaluate redundancy requirements for particular facilities such as air handling units, exhaust fans and decontamination system components (e.g., pumps & HEPA

filters)

- Assess location of BSL-3 labs in relation to BSL-2 support labs, offices and break rooms.
- Operational condition of doors.
- Inspect the logbooks and breakdown registers of all installations.
- Presence of an anteroom with/ without a shower.
- Storage provided for clean protective clothing and safety equipment
- Hands-free sink located near the exit of laboratory
- Office location outside of containment.
- Inspect signage for proper posting:
  a. Biohazard sign
  b. Agents used
  c. Names and telephone numbers for Laboratory In-charge and Biosafety Officer
- Special requirements such as required use of PPEs,
- Review the list of all mechanical controls and their locations
- Review start-up and shut down procedures in case of emergency

4 Evaluate maintenance frequency and review maintenance logs:

- Autoclaves
- BSC filters
- Centrifuges
- Door/ equipment locks
- HVAC balancing
- HVAC belts
- HVAC Motors
- Lights
- Plumbing.

5 Validation of Engineering Controls:

- Validate that extra capacity (approximately 20% more than required) is present on both supply and exhaust systems, and quantify the estimated spare capacity.
- Ensure single-pass airflow.
- Measure directional airflow, pressure relationships, air changes and record data.
- Directional air flow must be established from clean areas to contaminated areas. If multiple containment zones exist within a laboratory sequentially, more negative pressure differentials must be established so that the more contaminated spaces are maintained at a negative pressure with respect to less contaminated areas.
- Pressure differentials across doorways must be measured using a device calibrated against a primary standard. Ideally, at least -15 Pa should be maintained from clean areas to more contaminated areas.
- Develop HVAC system and electrical systems failure tests consistent with laboratory design parameters. Perform tests and record data. To verify correct operations these tests should include at a minimum:
  - Switching from Normal power to emergency power. UPS must be immediately on, there should be no lag during power failure. Generator must be functional in 1-2 minutes.
  - Switching from Emergency power to normal power.
  - Loss of supply fans (individual and in combination).
  - Loss of exhaust fans (individual and in combination).

- Building automation system (BAS) maintains operational set points during all scenarios and returns to normal operations.
- Upon reboot, BAS must retain operational set points.
- If an uninterrupted power supply (UPS) is installed, verify operation of relays.
- Provide UPS for BAS.
- Assess if UPS is operational and has sufficient backup time.
- Ensure that laboratories are maintained at negative pressure with respect to less contaminated areas.

- Assess HVAC equipment condition
  - Visually inspect:
    - Belts
    - Belt guards
    - Wiring
    - Duct supports and connections
    - air dampers
    - Bearings
    - Ductwork system workmanship, joint type, damage, etc.

- Ensure that motor operating temperatures are maintained within equipment specifications

- Ensure that interlock between supply and exhaust fan is operational

- Verify correct placement of biological safety cabinets with respect to supply and exhaust diffusers, doors and traffic patterns.

- Use smoke at the face of the cabinet to ensure that the air curtain is not being disrupted by supply or exhaust diffusers placed in proximity of the cabinet(s) or opening and closing doors and traffic patterns.

- Perform smoke tests to demonstrate directional airflow:
  - Doors
  - Vents
  - Windows
  - Autoclave
  - Other vented areas.

- Inspect and challenge door interlock systems and automatic door closers
  - Door closers are required
  - Ensure that doors automatically close and latch
  - Interlocks required
  - Check operability
  - Open and close doors in all possible sequences
  - Ensure that delay set points are tight enough to preclude inadvertent override of interlock.

- Test all alarms
  - HVAC Failure Alarm
  - Availability of airflow alarms showing if the room has gone positive under normal conditions or if door is open for greater than 20 seconds.
  - Availability of a visual indication for personnel to be aware if the room is under positive or negative pressure prior to entering into the lab
  - Review fire alarm annual documentation
  - Review security alarm annual documentation

- Discharge exhaust assessment:
  - Inspect rooftop landscape for re-entrainment opportunities
  - The emission from boiler, DG set, and other exhaust systems

should not mix with fresh air supply to the lab. For further details, users may refer to NIH guidelines (Wilson and Memarzadeh, 2006).

- Ensure that continuous flow centrifuges or other equipment that may produce aerosols are contained in devices that exhaust air through HEPA filters before discharge into the laboratory.
- Ensure that discharge of local exhaust ventilation devices is removed from air intakes to prevent re-entrainment.

- Verification of air changes per hour (ACPH) in containment spaces
  - ACPH is determined during design based on sensible and latent heat loads, contaminants, and odors that require containment space usage
  - Measure supply and exhaust air volumes using a device calibrated annually
  - Calculate ACPH; monitor trends
  - ACPH of 8-12 is recommended for BSL-3 lab, while 10-12 for ABSL-3 facility.
- Review biological safety cabinet (BSC) validation data
  - BSCs must be on an annual validation schedule
  - Verify that BSCs are located away from doors and vents
  - Verify that installation of BSC is correct for cabinet type.
  - Inspect HEPA filter installations
  - Review validation documentation for all exhaust HVAC HEPA installations
  - Verify that HEPA filters are on portable air vacuum systems at point of use and at the barrier
  - Visually inspect
  - Isolation valves for decontamination
  - Decontamination and challenge ports
  - Scanning access.
- Validate Mechanical, Electrical and Plumbing Services
  - Inspect for adequate illumination
  - Verify that circuit breakers are outside of containment
  - Backflow prevention for lab water system
  - Sinks and drains properly marked
  - Availability of emergency power for critical systems
  - Availability of hands-free emergency hand wash and eyewash
  - Availability of emergency shower
  - Caulking and sealing requirements for electrical devices such as conduits, boxes, lights, etc.
  - Validate provision for dedicated vacuum pump, if present
  - Inspect the effluent decontamination system.
- Validate autoclave availability, operations and bioseal integrity
  - Test interlocks
  - Confirm cycle test load
  - Visually inspect bioseal
  - Smoke test for testing bioseal
  - Validate maintenance of sterilization temperature of 121 degrees for 30 minutes.
- Validation of Effluent treatment

plant should be carried out

- All the critical (biosafety- related) installations of BSL-3 facility must be validated
- Additional environmental protection (e.g., personnel showers, HEPA filtration of exhaust air, containment of other piped services and the provision of effluent decontamination) is considered.

6 Administrative re-validation to facilitate Operation and Maintenance to ensure the safety of Occupants, Products and Environment:

Revalidation of certain containment components should be performed in normal routine without affecting the working of the containment facility. Nature and frequency depend on a number of factors. The following components essentially need to be revalidated, on an annual basis:

- Directional airflow
- Air velocity and No. of air changes per hour.
- Air Handling Unit
- Integrity testing of supply and exhaust HEPA filter housing and scanning of HEPA filters must be done annually. HEPA filters must be decontaminated prior to testing Revalidation of Particle Count
- Biological safety cabinets need to be validated at least annually and additionally after relocation of the cabinet, after electrical or mechanical maintenance and after HEPA filters are replaced.
- Differential Pressure
- Temperature & Relative Humidity
- HEPA Filter Integrity to indicate the necessity and frequency of replacing HEPA filters.
- Revalidation of other containment equipment like IVCs needs to be ensured.
- In addition:
  - Monitoring of the efficacy of autoclaves (quarterly internally) and revalidation at least annually
  - Detection of any visual leak in room perimeter
  - Detection of any leakage through entry/ exit doors, Pass box, Air-Lock doors etc.
  - Re-calibration of sensitive controllers and gauges
  - Record of calibration certificate of testing instruments
  - Monitoring the working of effluent decontamination system
  - Revalidation of critical components like integrity of room perimeter and duct work is necessary every time any major structural repair or modification in the structure or new installation of any critical equipment has been done.
  - All critical equipment in the laboratory should be under a maintenance contract and calibrated at recommended intervals.

All the testing and revalidation must be done by qualified and competent ISO/IEC 17025 accredited organizations.

ANNEXURE V

STANDARD OPERATING PROCEDURES (SOPs) FOR SPECIFIC CONSIDERATIONS FOR WORKING IN THE BSL-3 FACILITY

The Standard Operating Procedures (SOPs) must be developed by the Laboratory In-charge along with IBSC. A Biosafety Manual should also be prepared and adopted. The Biosafety and SOP manuals should be readily available to all users of the facility. There are several specific considerations for working in the BSL-3 facility, they have been broadly mentioned below:

Entry Procedures

Secured Entry

- Entry of new workers will be allowed only when accompanied by authorized personnel or once they pass the training.
- Controlled access entry is required through a fingerprint scan.
- Manual logging in log book required in the anteroom 1.
- Entry into Anteroom and Laboratory Space:
    - Location for manual logging in, head-cover, two layers of gloves: Anteroom 1
    - Location for Donning rest of PPE (PPE conforming to level 3 and above (e.g., Tyvek suit), N95, eye cover): Anteroom 2.

Donning SOP

- Put on two pairs of gloves, head-cover, shoe covers in Anteroom1
- Put on PPE conforming to level 3, N95 and eye cover in anteroom 2

*Make sure you are not wearing any sharp rings which will perforate the gloves.

Working within BSl-3 Laboratory

The use of good laboratory practices and appropriate microbiological techniques

- Being aware
- Proper pre-planning of procedures before entering
- Understanding the proper care and use of equipment within BSL-3
- Avoiding distractions as much as possible
- No work with infectious materials is conducted in open vessels on the open bench.

Use of Biosafety cabinets (BSC)

- Depending on the Class of cabinet, a suitable HVAC system
- Gauges should be checked to ensure the cabinet is operating within the validation parameters
- Use minimum equipment in the cabinet to allow for effective airflow.
- Keep grills clear and the sash at a proper level.
- Arm movement should be slow
- Waste container inside BSCs: A small plastic pail is used for liquid waste and for solid waste a biohazard bag is used (such as paper and plastic wrappers of serological pipettes).
- Waste containers outside the BSCs: All waste inside the BSCs are collected in a covered waste container lined with double biohazard bags on the floor adjacent to the BSCs.

SOP: Small Spill Response in BSCs

- Work should be halted as soon as possible after a spill occurs.
- Clean the spill as soon as safely possible in following way.
- Cover the spill with disinfectant adopted by lab and cover with paper towel to cover the entire spill.
- Leave for appropriate time and then pick up the paper towel and place in the biohazard bag in the BSC.
- Resume work.

SOP: Movement of culture

- No culture should be moved around in the BSL-3 laboratory without containing them in secondary container.

SOP: Small Spill Response outside BSCs

- Leave the room immediately, lock the door, post a warning sign and inform your Laboratory In-charge.
- Stop all work and inform all the workers in the BSL-3 and Leave the BSL-3 after proper doffing and inform others working in the lab or planning to work in the lab.
- All the workers must leave the BSL-3.
- If clothing is contaminated, remove and turn the exposed side of fabric in on itself and place in biohazard container.
- Wait at least 30 minutes before re-entering the lab to allow dissipation of aerosol created by the spill.
- During this time, review clean-up procedures, assemble material and contact the Biosafety Officer.
- Don fresh PPE
- Cover spilled material with an absorbent paper towel/tissue. Once the absorbent material is in place over the spill, wet the material with Lysol or formalin. Pour more around the spill. Use more concentrated disinfectant if the volume of material will significantly dilute the disinfectant.
- Allow 15 minutes contact time.
- Use forceps to place sharp objects into a sharp's container. Using an autoclavable dustpan and squeegee, tongs, etc., transfer all contaminated materials (paper towels, gloves, labware, etc.) to plastic bags and treat them as waste.
- Wipe surrounding surfaces with disinfectant to cover all splash areas. Wipe flat surfaces to remove any material that may have splashed out and settled on those surfaces.
- Place all contaminated materials into a biohazard bag for autoclaving.
- Complete an Accident Report form and also mention if one was exposed.

SOP: Glove puncture with contaminated instrument or pipette tip

- Two layers of gloves are to be used while experimentation and outer layer should be disposed of immediately after working at BSL cabinet.
- Decontaminate the top gloves with 70% ethanol and take it off inside the BSC.
- Spray more 70% ethanol on the inside gloves and take your hands out of the BSC and check for its integrity.
- If the inside gloves are not pierced, then put on the second pair of gloves and resume work.
- If the inside gloves are damaged, then leave the BSL-3 and don off according to SOP and wash your hands with soap and water. Check for any injury, if no injury, report the damaged gloves and resume work after proper donning.
- If skin injury is noticed, then do not squeeze the wound to induce bleeding
- Avoid the use of abrasive chemical soaps or disinfectant washes, as they can decrease skin integrity.
- Contact the laboratory director and

biosafety office and see the medical doctor immediately.

- Complete an Accident Report form and also mention if one was exposed.

Centrifuges and microfuge: Proper use

- Opening centrifuge rotor heads and caps must also be done inside a BSC.
- Rotors should be taken out from BSC in a closed container.

Sharps handling and disposal

- Use of hypodermic needles and Pasteur pipettes is restricted in the BSL-3 lab.
- If needles are to be used, "safe" or protected needle devices are recommended.
- Extreme care should be used to avoid auto-inoculation and aerosol generation. Contaminated sharps must be promptly placed in a puncture-resistant sharps container and decontaminated before disposal.
- Broken glassware must not be handled directly by hand.
- Plastic ware should be substituted for glassware whenever possible.

Autoclaving/Decontamination Procedures

- Decontamination should be done by the agent adopted as per lab SOP. For example: vesphene, lysol.
- All solid waste should be placed into a biohazard disposal bag and then autoclaved.
- All contaminated liquids are to be autoclaved after decontamination, preferably placed in closed, labelled, and leak-proof containers that have been surface decontaminated prior to removal from the containment zone.
- Material to be removed from the facility shall be properly decontaminated by autoclaving or by chemical disinfection. Reuse should be avoided. However, if essentially needed, reusable containers shall be decontaminated by immersion in an appropriate disinfectant for recommended time (care should be taken to fill completely). The items will be then drained and autoclaved out of the facility.

Facility upkeep and cleaning

- Researchers will perform all daily housekeeping routines within the BSL-3 lab, including trash removal. All the cleaning and decontamination procedures shall be performed only by individuals authorized to work in the BSL-3 facility.
- Large equipment, such as incubators and centrifuges, will have inner and outer surfaces damp-wiped with disinfectant on a routine basis.
- Water baths: shall be rinsed periodically with a suitable chemical decontaminant. It is recommended to add copper sulphate to the water.
- Lab notebooks shall not be brought into the containment section of the lab. If essential, any notes/papers to be taken outside should be decontaminated by treating with a suitable agent like vesphene and then, taken out through autoclave/ fumigation chamber/Airlock.

Exit procedure

- Secure infectious materials
- Waste disposal/decontamination
- Disinfect work surfaces
- Doffing and its proper disposal: Disposable PPE should be placed into a biohazard container
- Hand washing
- Exit.

Doffing SOP

- Decontaminate your gloves and shoe covers as per laboratory SOP like with vesphene/Lysol/ 1% Sodium Hypochlorite solution in Anteroom 2.
- Take off the bodysuit so that no outside portion of gown touches the inside clothing, remove gown, and place it in biohazard bag.
- Remove first pair of gloves and place it in biohazard bag.
- Remove eye protection and spray with disinfectant and place it in the storage cabinet.
- Remove N95 mask and discard.
- Before entering the Anteroom1, remove shoe covers and last pair of gloves and discard them in biohazard bag.
- Wash and sanitize your hands. Water/air shower as postulated in the Laboratory SOP.
- Record your exit time in the log book in the Anteroom 1 and exit.

Storage of GE organism/Hazardous microorganism/Infectious material

- GE organism/Hazardous microorganism/ Infectious material should be clearly labelled and stored in isolation in such a way that it cannot be mixed with other materials.
- All storage areas should be clearly labelled and limited to authorized personnel only.
- All personnel who have access to the storage areas should be adequately trained on the labelling, storage and disposal procedures.
- Where a storage area is used to store multiple samples of GE organisms, each item should be stored separately in a sealed, labelled container such as a primary container for shipment.
- Proper care should be taken to maintain appropriate storage conditions, including temperature.
- In the event of any suspected unintentional release of GE organisms from storage, emergency action plans should be adopted, and competent authority should be informed.

Transport of GE organism/ Hazardous microorganism/ Infectious material

- GE organism/Hazardous microorganism/ Infectious material within the country must be packaged to withstand breakage and leakage of contents and be labelled, as specified in the International Air Transport Association's (IATA) Dangerous Goods Regulations and *"Regulations and Guidelines for Recombinant DNA Research and Biocontainment",* as updated time to time and available on IBKP.
- All shipments should be recorded.
- Import/export of GMO/HMO shall be approved by IBSC/RCGM as per the extant guidelines.

Incident Response Procedures/ Emergency Response Measures/ Post-exposure practice and procedures

- Spills and accidents that result in overt or potential exposure to infectious material should be immediately reported to the Laboratory In-charge and Biosafety Officer.
- Medical evaluation, surveillance, and treatment are provided as appropriate, and written records are maintained.

Contact Information/Responsible Official/Biosafety Officer

- Check that the phone is operational and emergency numbers are posted.
- Do not work in the facility unless a means to summon help in an emergency

situation is available.

- Any problems should be reported to the Laboratory In-charge.

Safety SOP

- Identification of responsible official and Biosafety Officer for BSL-3 facility.
- Certification of all personnel working within containment and the process followed to certify them.
- Use, storage and disposal of Personal Protective Equipment.
- Documented limited personnel access to facility.
- All new research personnel must get the appropriate training by IBSC designated training cell, before beginning to use the facility
- Procedures to enter facility for maintenance.
- Hand washing procedures are in place.
- Ensure use of mechanical pipetting devices. No mouth pipetting.
- Use of sharps prohibited unless absolutely required and then use should be managed by protocol.
- Procedures in place to minimize production of aerosols.
- Decontamination procedures are in place.
- Training program is in place, and documentation is available for training and refresher courses for all personnel, including maintenance staff working in the BSL-3 facility.
- A biosafety manual specific to the laboratory must be prepared and adopted by the facility.

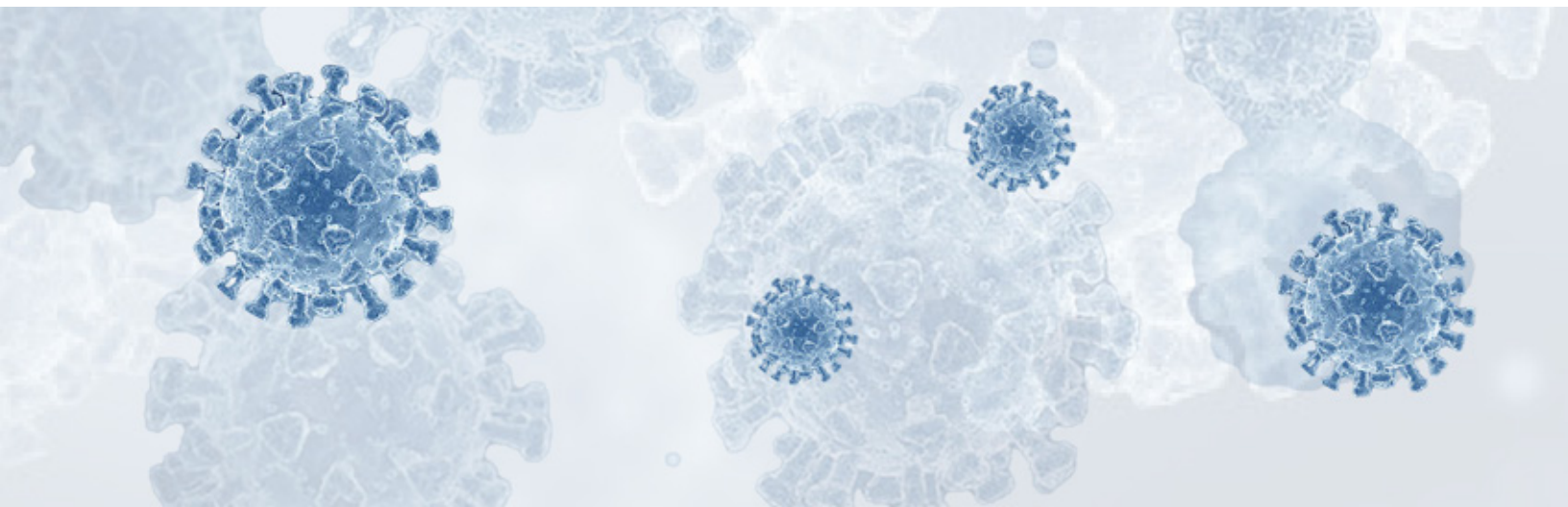
Technical SOPs must be written and be available.

The following records have to be maintained

- Training and refresher training to be documented; records to be kept on file.
- Annual inventory of stocks of pathogens, toxins, and other regulated infectious material in long-term storage to be maintained, including location and risk group.
- Provision for detection of a missing sample in a timely manner.
- Map and physical specifications of BSL-3.
- Records of regular inspections of the containment zone and corrective actions to be kept on file.
- A record of all individuals entering and exiting the containment zone to be maintained and kept on file.
- Records of routine decontamination and its verification
- Records of incidents and the responses.

Validation

- Facilities must be revalidated annually.
- BSCs should be preferably revalidated annually or after major repair/ location change.



ANNEXURE VI

APPLICATION FORMAT FOR CERTIFICATION OF THE BSL-3 FACILITY

For certification of the BSL-3 facility, entities (such as Institutions/ Universities/ S&T organizations/ Educational organizations/ Societies/ Autonomous bodies) falling under or related to the Central Government, are required to submit the application to the concerned line Ministry of the Government of India. Till the constitution of the Expert Committee for certification by respective Line Ministry, certification of BSL-3 facility may be considered by the Expert Committee for Certification of BSL-3 facility, constituted by DBT for the purpose.

For Certification of BSL-3 facility of entities falling under or related to the State Government: those pertaining to the Ministry of Health shall be dealt by DHR, ICMR/DoH&FW, while Certification of facilities established in other State Government institutions may be undertaken by DBT. In respect of all other entities, i.e. Non-Governmental Organizations undertaking research and development activities, application should be submitted to the RCGM, DBT. In both cases, the following application format (basic information and application checklist) should be used to obtain necessary certificate. Submission of incorrect or incomplete information may delay or disqualify granting the certification and it may attract penal actions as per those mentioned in the Environment (Protection) Act, 1986. Additional information may be required, and will be notified on a case-by-case basis. The certificate will be valid for a period of 3 years from the date of issue, with re-validation of essential parameters of the facility on an annual basis. Thereafter, the certificate needs to be renewed. The certificate holder should ensure to comply with the conditions of the certification.

1 Application format:

A Basic Information

Organization details

Name of organization:

Address:

Contact No.:

IBSC registration details:

Applicant details

Name of the PI:

Designation:

Address:

Telephone No.:

Fax No.:

E-mail:

Application type

New	☐	Renew	☐

If applying for renewal of certificate, please indicate the respective controlling ministry certification number: _____

Status of laboratory accreditation by NABL or equivalent agency (applicable for testing laboratory):

Yes	☐	No	☐
If Yes, Please provide details:			

B Application checklist for BSL-3 Facility (Documentation to be submitted by the Laboratory In-charge for examination/inspection of the facility by the committee)

B.1 General Checklist

A List of staff with details: position and responsibilities who work in the BSL-3 facility and their BSL-3 training records

B Does the lab perform competency assessments of the staff?

☐ Yes ☐ No

If yes, how? .....

C Laboratory facility Layouts and Flow charts of:

- Blueprint of laboratory facility layouts [pdf copy] with drawing of the campus denoting the location of the laboratory
- Facility-layout showing flow chart for:
  - Clean material entry
  - Movement of samples for processing for various laboratory tests
  - Entry and exit & movement of Lab staff in the laboratory
  - Liquid & solid waste management procedure.

D Certificate from the Contractors/Executing agency with regards to the

following:

- Demonstrated commissioning of physical infrastructure of laboratory
- On-site equipment functionality
- Declaration regarding “Constructed as per design plan in concordance with PIs”.

E Detailed review from Contractors/executing agencies for:

- Surface specifications (able to withstand disinfectants, impact resistant, etc.)
- AHU, exhaust and HEPA filter housing is as per the risk assessed by the PI
- Laboratory services (types of drainage traps, sealing of penetrations, etc.)
- Biosafety cabinets [numbers, types and their locations on the layout of the facility, recent BSC certification date]
- Validation records of various installations [On-site equipments] in BSL-3 laboratory.

F Any external review done to ensure the suitability of:

- Engineering Controls: HVAC, AHUs, Building Management System (BMS) [In brief]
- Decontamination and Waste management programs [Autoclaves, liquid waste management: details of Biological Liquid Decontamination facility or Kill tank]
- Facility maintenance SOPs and PERT chart for maintenance, signage with regards to engineering facility: physical, chemical & electrical
- AMC of the facility and current status
- Procedure for documentation and record retention with regard to engineering facility
- Maintenance of facility [List of manuals, log books, records, etc.]
- Redundancy requirements [E.g.: Decontamination system/AHUs].

G Report of Expert Committee involved in laboratory validation, to ensure adequacy for meeting the requirements:

1. Objectives and mandates of the laboratory and list of documents prepared for operation of BSL-3 facility:
2. Procedure of Administrative Controls for Biosecurity
3. Name of the Biosafety Officer:
4. Names of Institutional Biosafety Committee (IBSC) Members:

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

5. Laboratory validation documents, facility documents as per the laboratory mandate administrative controls PPE, in-house staff training programs & SOPs with regards to laboratory activities
6. Documentary proof of risk-assessment of the laboratory with respect to biosafety and biosecurity
7. Fitness certificate of all laboratory essential engineering systems, stand-alone equipments
8. Analytical and diagnostic performance of tests performed in the laboratory
9. Emergency management plan/Emergency equipment and response protocols [& natural disaster management plan]
10. Medical surveillance of staff [who are authorized to work in BSL-3]
11. Physical & digital security of facility
12. Facility inventory [list of equipment's & maintenance records, samples & isolates storage]
13. Memorandum of Understanding (MOU) along with valid Consent to Operate (CTO) with State Pollution Control Boards (SPCBs)/Pollution Control Committees (PCCs), as applicable, for compliance towards Biomedical waste decontamination and disposal.
14. Integrated pest control program
15. Videography of the facility [depicting various controls in the facility].

B.2 Checklist for evaluation of Facility design

Requirements of Facilities		Yes	No	Remarks
1	Proper engineering controls are being used and are functioning adequately as designed.			
2	Access control: Only authorized persons are allowed to enter the laboratory working areas.			
3	The facility must be a fully enclosable space, bounded by walls, doors, windows, floors and ceilings, which permit operation of the facility under negative pressure.			
4	The facility must be constructed to enable gaseous decontamination of the whole facility.			
5	All facility penetrations must be fitted with seals to minimize air leakage.			
6	All windows in the facility must be closed and sealed.			
7	The facility boundaries (walls, windows, doors, floors, ceilings etc.) must be constructed to prevent the incursion of pests.			
8	Where present, liquid drainage exits must be protected against entry and exit of invertebrates or other animals by the use of screens, liquid traps or an equivalent effective method. Where a screen is used, the apertures of the screen must be small enough to prevent entry or exit of invertebrates or other animals.			

9	The laboratory must be separated from areas that are open to unrestricted traffic flow within the building. Additional separation may be achieved by using a laboratory at the blind end of a corridor, a partition and door, a double-door system where entry to the laboratory must be through an ante-room or airlock. The Panels should be fire-rated in Partition.			
10	Airlock doors must be self-closing and fitted with seals at the top, bottom and both sides of the door. Airlock doors must contain a viewing panel unless the airlock functions as a shower airlock.			
11	Where the facility shares an airlock with an ABSL-3 animal or invertebrate facility, or if animals or invertebrates are handled within the facility, any openings in the walls or ceiling, such as ventilation inlets and outlets must be screened. The screens must be fixed and sealed against their mounting. The apertures of the screen must be small enough to prevent entry or exit of invertebrates or other animals.			
12	Provision must be made for viewing work areas from outside the facility.			
13	Walls, ceilings and floors are smooth, easily cleanable, impermeable to liquids and resistant to the chemicals and disinfectants.			
14	Adequate illumination is ensured for carrying out all activities. Undesirable reflections and glare are avoided.			
15	Laboratory furniture is sturdy and open spaces between and under benches, cabinets, and equipment are accessible for cleaning.			
16	Bench tops are impervious to water and resistant to disinfectants, acids, alkalis, organic solvents, and moderate heat.			
17	Biological safety cabinets for handling of infectious microorganisms of risk group 3 are available.			
18	Attention is paid in designing laboratory and assigned certain types of work that are known to pose safety problems. a) Formation of aerosols b) Overcrowding and too much equipment.			
19	Sufficient space provided for the safe conduct of laboratory work and for cleaning and maintenance.			
20	Piped gas supplies to the facility must have reverse flow prevention on outlets located within the BSC.			
21	There must be a ventilation system that establishes a negative pressure into the laboratory so that there is a directional airflow from the corridor or the basic laboratory to the working area of the containment laboratory. Personnel must verify that proper direction airflow (into the laboratory) is achieved.			
22	Cup (U Traps) sinks acting as vent.			

23	The work area must be maintained at a negative air pressure of at least 50 Pa compared to outside the facility when doors of the airlock are closed. When either door of the airlock is open between adjacent areas, a differential pressure gradient of at least 15 Pa should be maintained to prevent back-airflow from more contaminated to less contaminated areas.			
24	The work area must be equipped to measure and display the pressure difference between the facility and the areas adjacent to the facility. The display must be located so that it can be read immediately before entering the facility.			
25	The facility must be equipped with an alarm that will alert relevant persons both inside and outside the facility and be immediately activated when the differential pressure between different containment zones of the facility is less than 5 Pa.			
26	Provisions for autosensing alarms for fire and other emergencies that need evacuation.			
27	Backup power source in event of unexpected power failure/ shutdown.			
28	The facility must have an emergency stop button for the ventilation system, which is easily accessible in case of an emergency. The emergency stop button must operate independently of the main ventilation control and main facility pressure control system such that emergency isolation of the ventilation can be implemented in the event of central control malfunction.			
29	Supply or replacement air to the facility is HEPA filtered.			
30	The exhaust filter must be a HEPA filter and must be tested by qualified person. The exhaust HEPA filter must be mounted in a gas-tight housing, with sealed access doors and the ductwork between the facility and the HEPA filter housing must also be gas-tight. The design and location of the filter housing must allow for access to and integrity testing of the HEPA filter.			
31	Access to the laboratory area should be designed to prevent entrance of free-living arthropods and other vermin.			
32	Wash-basins are provided in each laboratory or any other means of decontamination of hands provided.			
33	The following water supplied to the facility must be protected against backflow: a) laboratory sink and equipment outlets (including autoclaves) b) outlets within a BSC or other aerosol containment equipment.			
34	Designated storage or hanging provisions for personal protective equipment available in facility.			
35	Eyewash equipment is provided.			

36	The international biohazard warning symbol and sign are displayed on the doors of the rooms where microorganisms of Risk Group 3 or higher risk groups are handled.			
37	Shower facility, wherever mandated or required as per risk assessment, must be available in the facility before exit.			
38	Class II/III biological safety cabinets are placed in proper place.			
39	Incinerators, if used, must have dual combustion chambers.			
40	An autoclave, preferably of double door barrier with interlocked doors with the inner door opening to the facility and outer door opening externally to the facility is available.			
41	Refrigerators, freezers, incubators, etc. that contain biohazardous materials for storage must be labelled with a biohazard symbol.			
42	Proper wastewater treatment facility available, working properly.			
43	Fire protection: facility equipped with Fire detection and monitoring system with alarm facility, along with provision of manual fire extinguisher.			
44	Open penetration in walls, ceiling, floor, etc.			
45	Wiring or tubing through door openings.			
46	First Aid areas are suitably equipped and readily accessible.			
47	Antimicrobial and antiseptic agents available for immediate first aid.			
Additional requirements for IBSL-3		**Yes**	**No**	**Remarks**
1	The arthropod facility should be provided with an access room. The access room should be fitted with insect-control units for example an electric insect-control device or an ultra-violet insect zapper.			
2	Access room doors should be sealed to be arthropod-proof.			
3	If risk assessment requires additional mitigation measures for arthropod containment, an anteroom may be provided with a sink and vacuum system to enable personnel to remove any arthropods, eggs or larvae from their person before leaving the facility.			
4	For additional details, refer to *"Guidelines and Standard Operating Procedures for Research on Genetically Engineered Insects"*, as updated time to time and available on IBKP.			

B.3 Checklist for evaluation of Facility operation

Operation checklist		**Yes**	**No**	**Remarks**
1.	Measures are available to restrict access to the laboratory.			
2.	Periodic inter-inspection and audit of the facility are available.			
3.	Record keeping of biosafety policies and procedures (SOPs) for the laboratory (facility) including training of laboratory and maintenance staff.			

4.	Record keeping of SOPs for document retention, maintenance and lab procedures.			
5.	Inspect signage for proper posting.			
6.	Biohazard sign.			
7.	Agents used.			
8.	Names and telephone number of Laboratory In-charge and Biosafety Officer.			
9.	Eating and drinking were not observed and no food/drinks were stored in work areas.			
10.	Personal Protective Equipment is clean, available and used appropriately; not worn outside of lab.			
11.	Biosafety cabinets (BSCs) are field-tested and validated annually.			
12.	Autoclaves are maintained, calibrated and validated.			
13.	Aerosol-generating activities (sonication, vortexing, homogenizing) are performed inside BSC for risk group 2 microorganisms.			
14.	Centrifuge safety cups or sealed rotors are used to centrifuge RG-3 microorganisms.			
15.	Personnel employ safe handling of sharps.			
16.	Work areas are decontaminated regularly after work and after known contamination.			
17.	Personnel know how to clean up a spill.			
18.	Waste segregated in proper colour coded containers.			
19.	Culture stocks and other regulated waste are properly decontaminated before disposal.			
20.	Materials decontaminated outside the laboratory are transported in closed, durable, leak-proof containers according to local rules and regulations.			
21.	All biohazardous waste containers are closed or covered when not actively used.			
22.	Autoclave bags with biohazard symbols are available and used for decontamination.			
23.	Lab personnel are up to date on required safety training and lab specific training.			
24.	Personnel know symptoms associated with organisms used in the lab.			
25.	Personnel know how to handle exposures and to report accidents immediately.			
26.	Review start-up and shut-down procedures in case of emergency			
27.	Evaluate maintenance frequency and review maintenance logs for Autoclaves, BSC filters, Centrifuges, Door/ equipment locks.			

28.	HVAC balancing, HVAC belts, HVAC Motors, Lights, Plumbing.			
29.	Appropriate laboratory operation manual is accessible to personnel.			
30.	Record of HVAC system and electrical systems failure tests.			
31.	Record of smoke tests to demonstrate directional airflow. a. Doors b. Vents c. Windows d. Autoclave e. Other vented areas			
32.	Test for all alarms.			
33.	Record of work is duly registered in the daily register available.			
34.	Personnel know the process of registering and reporting in case of accidents			
35.	Verification of ACPH. There should be 8-12 air-changes per hour for laboratory and 10-12 for ABSL-3.			
36.	Record of Biological Safety Cabinet (BSC) validation data.			
37.	A training program is available for fresh candidates.			
38.	Record of medical examination of all laboratory personnel including past medical history is available.			
39.	Baseline serum sample is stored for future reference.			
40.	Immunocompromised personnel are not employed.			
41.	Medical contact card is available for all personnel.			
42.	Laboratory monitoring plan is available and working including periodic surveillance.			
43.	Inspect Mechanical, Electrical, Plumbing Services.			
44.	Proper waste management plan available and is adopted.			
45.	Validate autoclave availability, operations and bioseal integrity.			
46.	All instructions related to waste management are posted inside and outside of laboratory and must be visible clearly.			
47.	Inspection of personnel showers, HEPA filtration of exhaust air, containment of other piped services and the provision of effluent decontamination.			
48.	Hand-washing sink available near laboratory exit.			

B.4 Current research activities/projects involving work in the BSL-3 facility

Name of RG-2/RG-3/Exotic microorganisms being handled (as applicable)	Name of RG-2/RG-3/Exotic microorganisms being stored (as applicable)

2 Review of the application

The concerned line Ministry of the Government of India may constitute an Expert Committee for certification, which should have a representative from CPCB, subject matter experts experienced in establishing/working in BSL-3 facility and engineers with experience of installation, testing, commissioning and maintenance of the BSL-3 facility to review the application for certification and recommend certification of newly constructed as well as existing BSL-3 laboratories after review of all the required/relevant documents. The committee shall examine the documentation submitted by the Laboratory In-charge. The committee also reviews the documents of validation done by qualified and competent ISO/IEC 17025 accredited organizations.

If desired, the committee will recommend a site visit for inspection of the facility. An inspection checklist (see below) for evaluation of facility design and operational practices within the facility should be filled at the time of inspection. Laboratory In-charge must be present at the time of inspection. The filled checklist, duly signed by the inspection committee, shall be considered by the Expert Committee while evaluating the application. The recommendations of the Expert Committee (as per ***Annexure VIII***) must be submitted to the Controlling Ministry or RCGM, DBT along with all other documents. Based on the above recommendation and substantiating information, Certificate of compliance for the BSL-3 facility shall be issued by the respective Line Ministry or RCGM, DBT. The same shall be communicated to RCGM, DBT for information, in case issued by other Line Ministry.

2.1 Inspection checklist

(Note: Only a single checklist should be submitted even if the facility is inspected by more than one person.)

i. Is general checklist and checklist (as per B.1, B.2 and B.3 in application format) duly filled post inspection?	Yes ☐	No ☐
ii. Inspection Report & Checklist attached? (Note: Only a single checklist should be submitted even if the facility is inspected by more than one person.)	Yes ☐	No ☐

iii. Does the facility meet all requirements contained in this guideline?	Yes ☐	No ☐
If No, please provide details of:		
a. Which requirements in the relevant guidelines are not met; and b. What strategies do you suggest to manage any risks that may arise or reasons why it is considered that the requirement or condition is not necessary to achieve containment? -------Enclose separate sheet, if required-------		
c. Please provide any other information that may assist the controlling ministry or RCGM in making a decision about this application. -------Enclose separate sheet, if required-------		

Declaration of the Organization seeking certification

This declaration must be completed and signed by the utmost authority of the organization, or a person with the authority to sign on behalf of the organization.

I, ... **(NAME AND DESIGNATION OF THE COMPETENT AUTHORITY)** of ..... **(NAME OF THE ORGANIZATION) DECLARE THAT:**

- I am duly authorized to sign this declaration.
- I have extended full cooperation to the inspector(s) during their visit.
- The information supplied in this form and any other attachment is true and correct; and,
- I am aware that the making of a false or misleading statement may be punishable by imprisonment or a fine under the Environment (Protection) Act, (1986).

Date **Name of authority with official seal**

Place

Declaration of the Expert Committee constituted for the purpose

I DECLARE THAT:

- I have personally inspected the facility on .....
- I have recorded the observation in this form during the visit.
- My decision was not influenced and full support was extended to me during inspection.
- I attest that the information contained herein is accurate and complete to the best of my knowledge and belief.

Date **Name of Chairperson of Expert Committee**

Place **with complete designation**

Declaration of the DBT Nominee

I DECLARE THAT:

- I have personally inspected the facility on .....
- I have recorded the observation in this form during the visit.
- My decision was not influenced and full support was extended to me during the inspection.
- I attest that the information contained herein (in application as per ***Annexure VI*** of the *National Guidelines for the Establishment and Certification of Biosafety Level-3 (BSL-3) containment facility, 2024* is accurate and complete to the best of my knowledge and belief.

Date **Name of DBT Nominee, IBSC**

Place **with complete designation**

ANNEXURE VII

UNDERTAKING BY IBSC

IBSC, ... **(NAME OF THE ORGANIZATION) DECLARES THAT**:

We have verified the documents submitted as per ***Annexure IV***: Validation procedure for BSL-3 laboratory and ***Annexure VI***: Certification of BSL-3 facility of *National Guidelines for the Establishment and Certification of Biosafety Level-3 (BSL-3) containment facility, 2024*.

- We have personally inspected the facility on .....
- We have recorded the observation(s) in this form during the visit.
- Our decision was not influenced and full support was extended to us during the inspection.
- We attest that the information contained herein is accurate and complete to the best of our knowledge and belief.

Date

Place

Chairperson, IBSC with complete designation/official seal

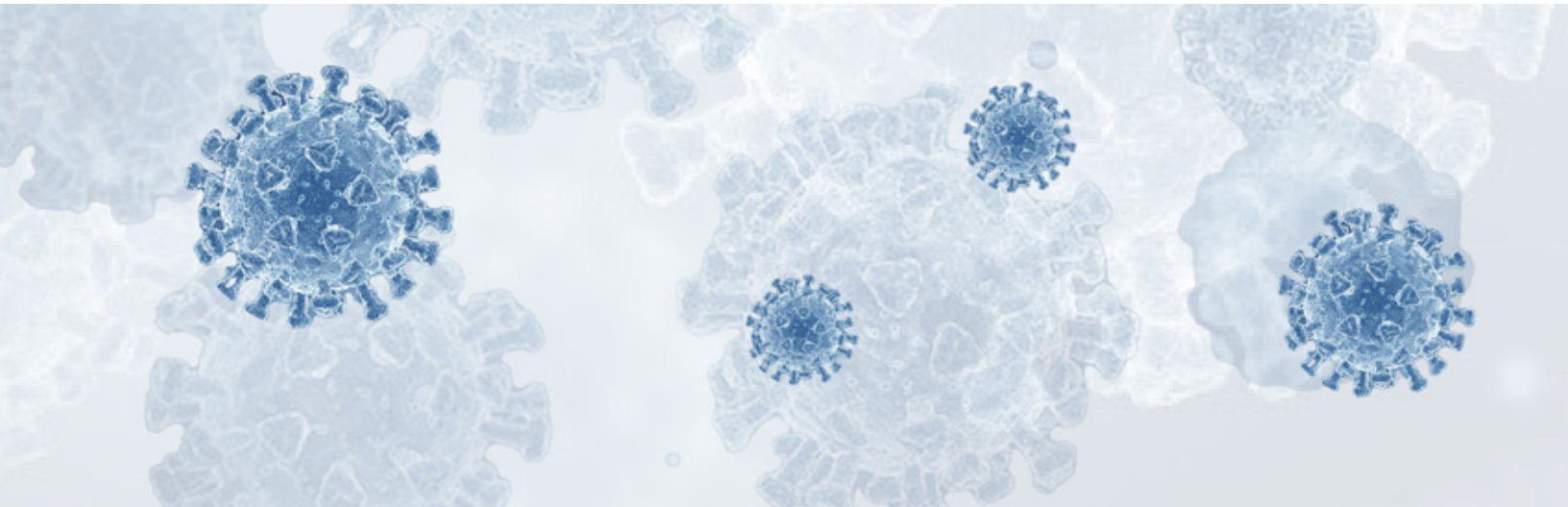
DBT Nominee

Member Secretary

Biosafety Officer

Outside Expert

Internal Member



ANNEXURE VIII

REPORT OF THE EXPERT COMMITTEE CONSTITUTED FOR CERTIFICATION BY THE LINE MINISTRY

..... **(Name of the Organization)** submitted the documents for certification of BSL-3 lab at ..... The documents were reviewed by the Expert Committee. The comments of the committee are as below:

A Facility design:

i Layout and design of facility: Appropriate/Inappropriate

ii Facility commissioning and validation report: Yes/No

iii Operations SOP (Entry & Exit/AHU/Showers/maintenance/Breakdown): Yes/No

iv Maintenance records: Available/Not available.

B Equipment:

i Necessary Equipment: Available/Inadequate

ii Commissioning and validation report: Yes/No

iii Log books: Yes/No

iv SOPs (including maintenance & breakdown): Yes/No

v Maintenance records: Available/Not available.

C Personnel:

i List of persons authorized to work: Available/Not available

ii Competency and training (including biosafety): Yes/No

iii Health assessment (vaccination records): Yes/No

iv Biosafety and Biosecurity measures: Appropriate/Inappropriate.

D Workflow:

i Objectives of the lab: Defined/Not defined

ii Experimental SOPs: Yes/No

iii Sample storage protocols and inventory management: Yes/No

iv Incident reporting mechanism: Yes/No

v Bio-medical waste management including sharps (policy/log): Yes/No.

E Regulatory:

i IBSC constituted and Biosafety Officer appointed: Yes/No

ii Pollution Control Board approval: Yes/No

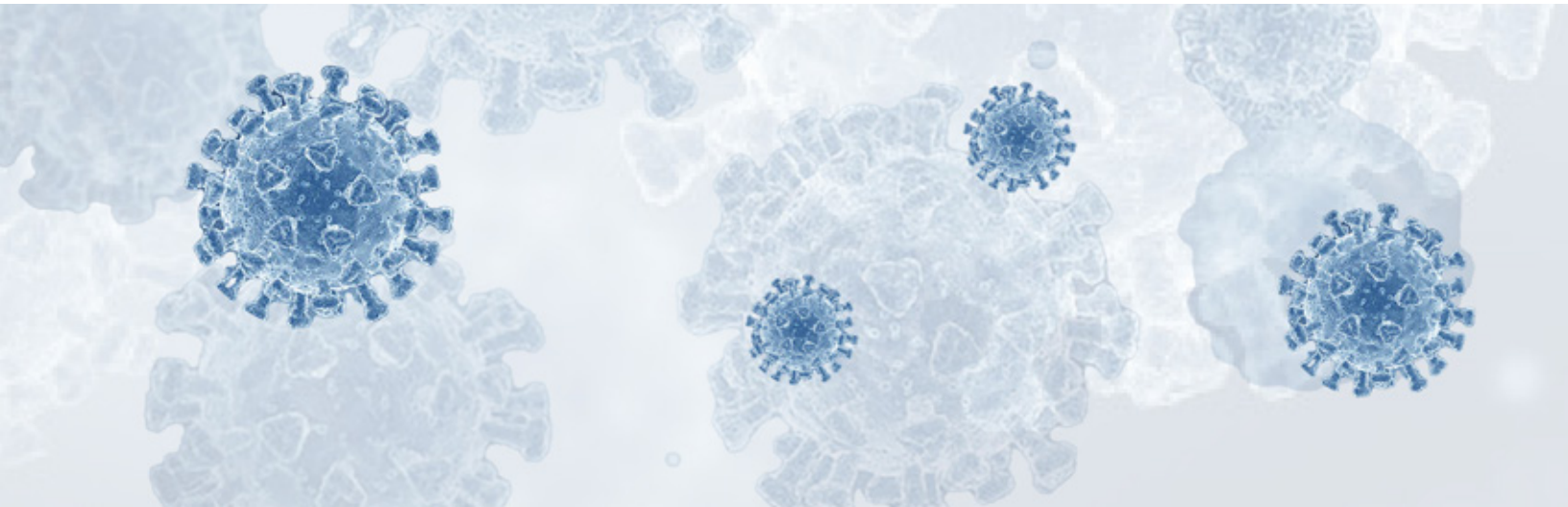
iii Fire safety

iv Audit.

Remarks, if any:

Decision: Recommended/Not Recommended

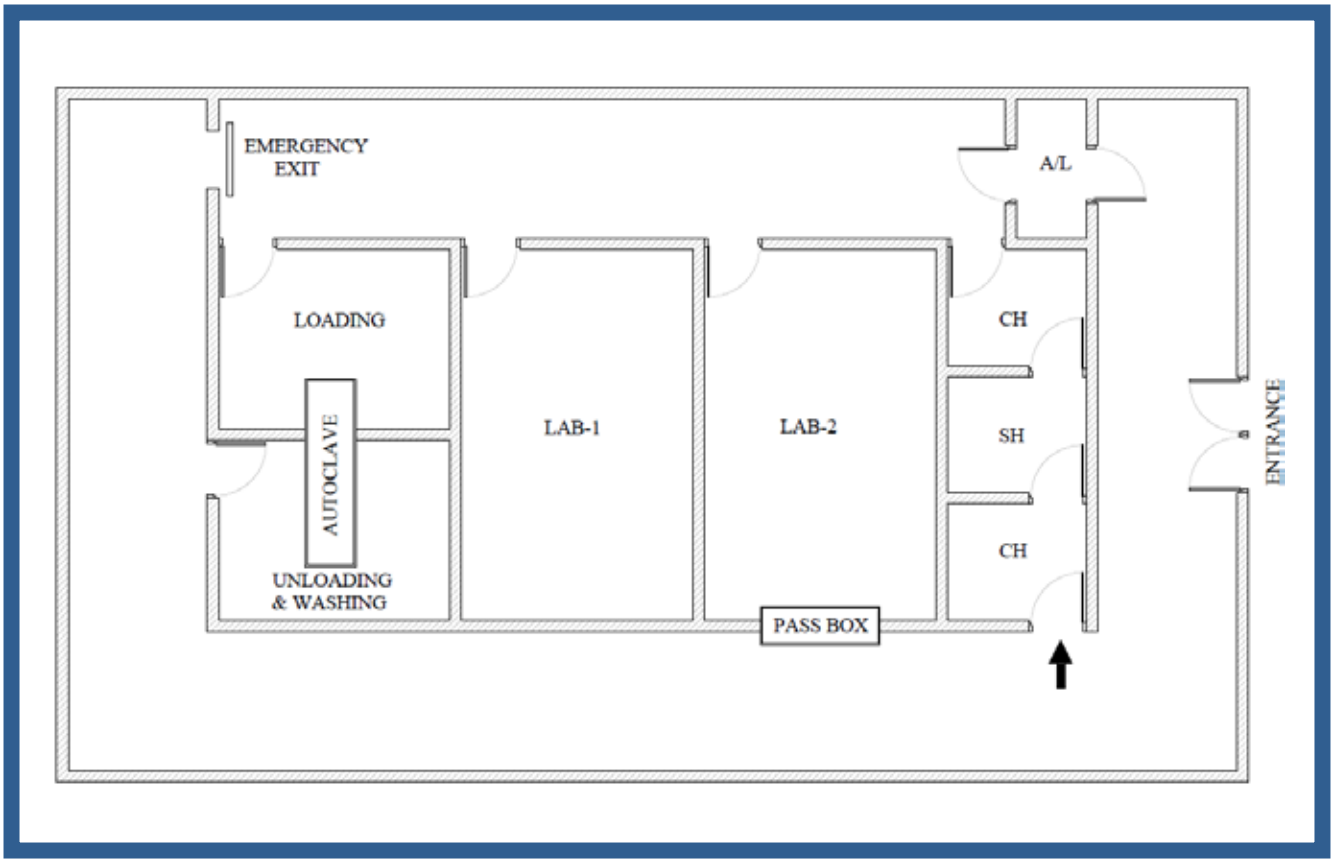
In case not recommended, the Laboratory In-charge is advised to read the detailed report of assessors attached herewith and take necessary remedial measures before resubmitting the application for certification of the BSL-3 lab.



ANNEXURE IX

CONCEPTUAL BSL-3 DRAWINGS

MODEL 1



Legend:

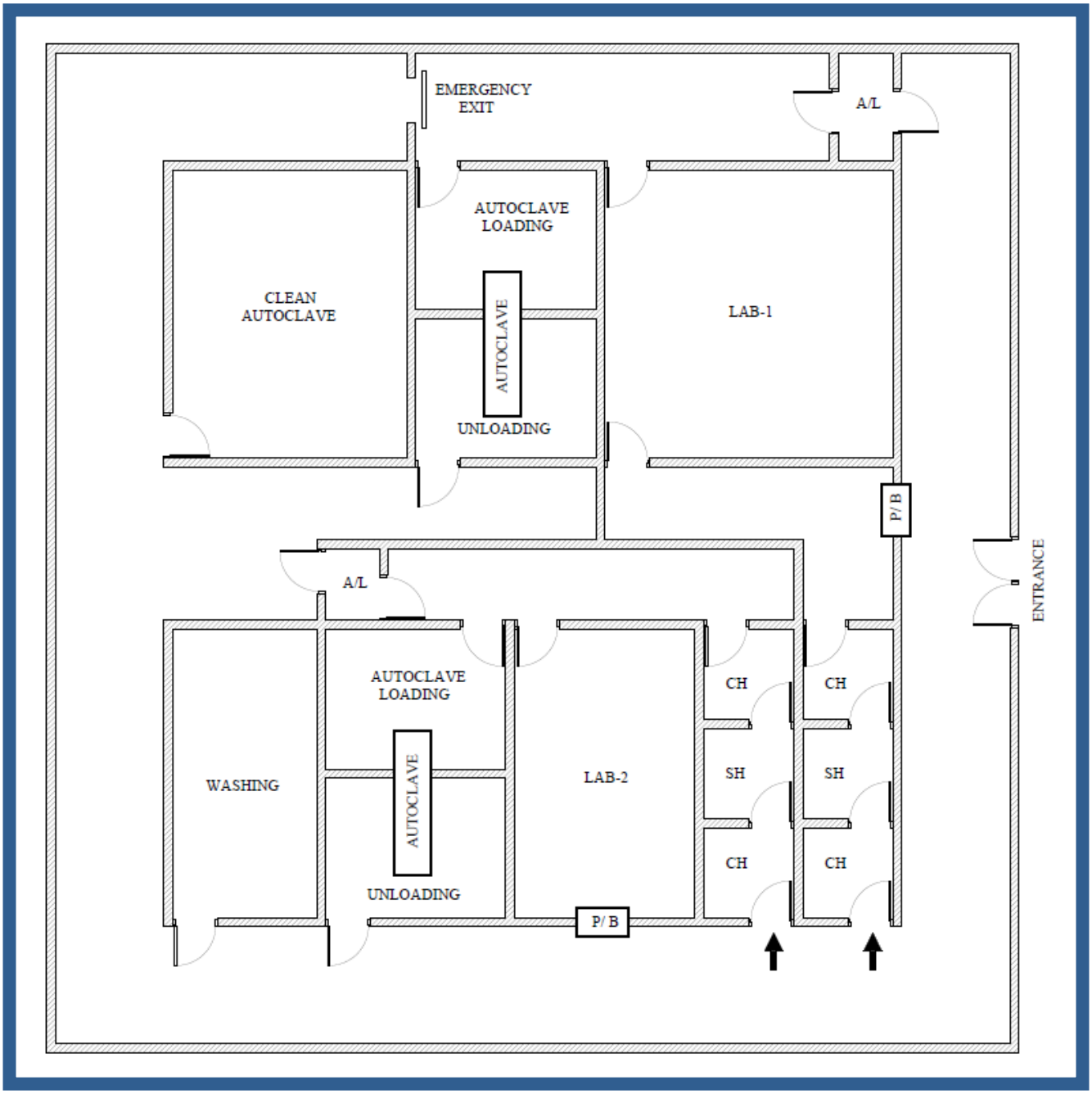
CH: Changing Room

SH: Shower

PB: PassBox

A/L: Airlock

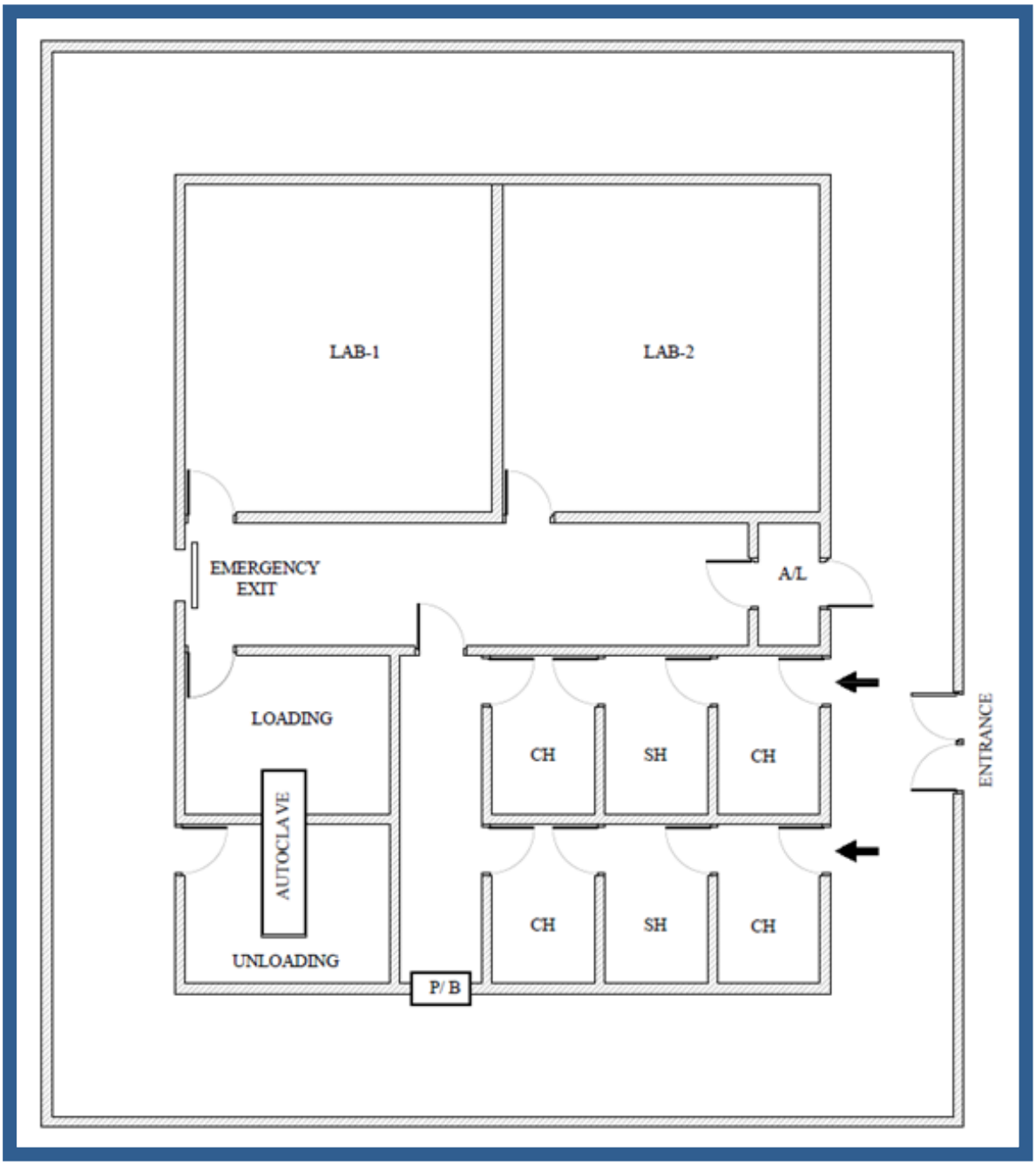
MODEL 2



Legend:

CH: Changing Room
SH: Shower
LAB-1: Animal Side
LAB-2: Lab Side
PB: PassBox
A/L: Airlock

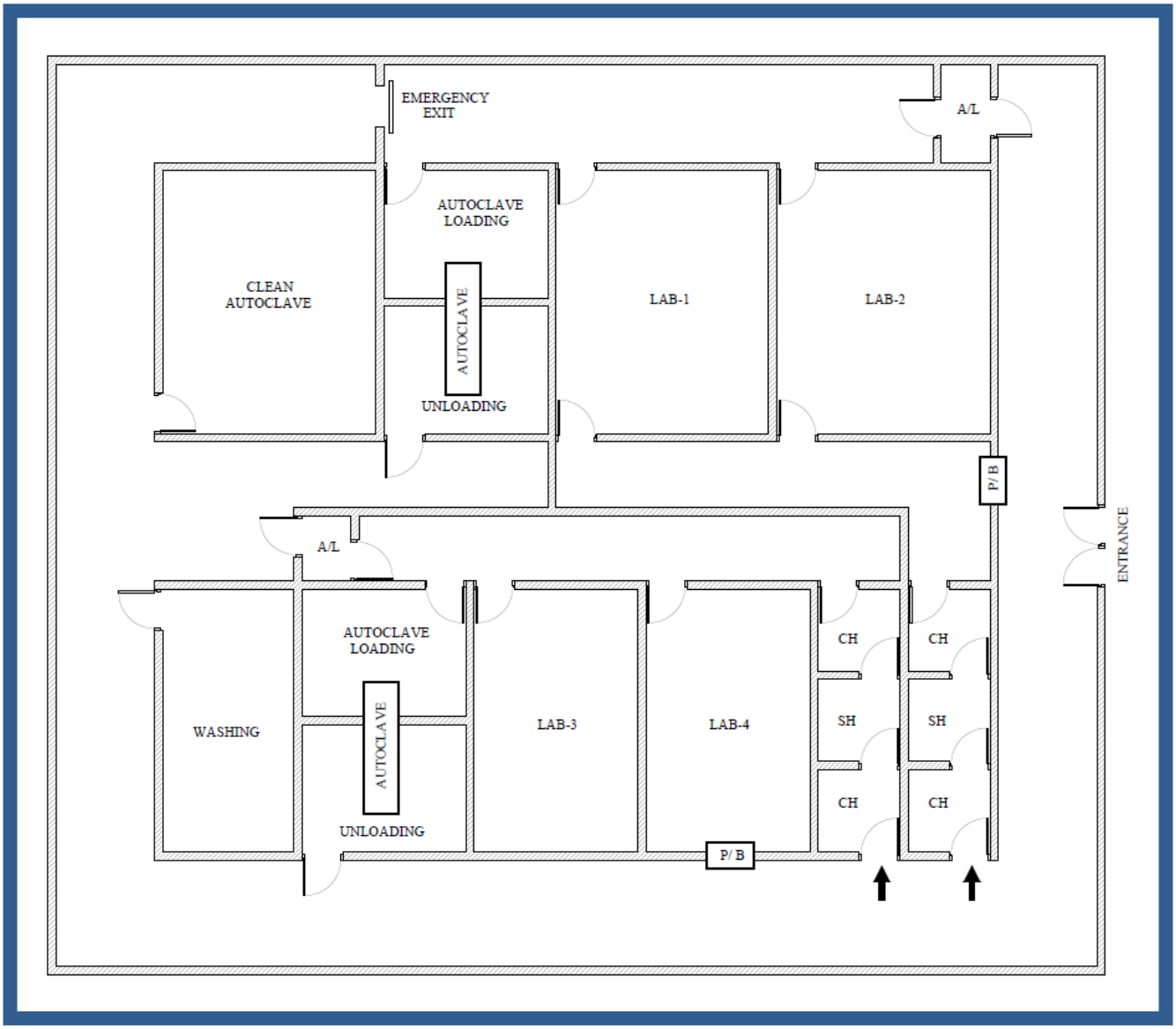
MODEL 3



Legend:

CH: Changing Room
SH: Shower
PB: PassBox
A/L: Airlock

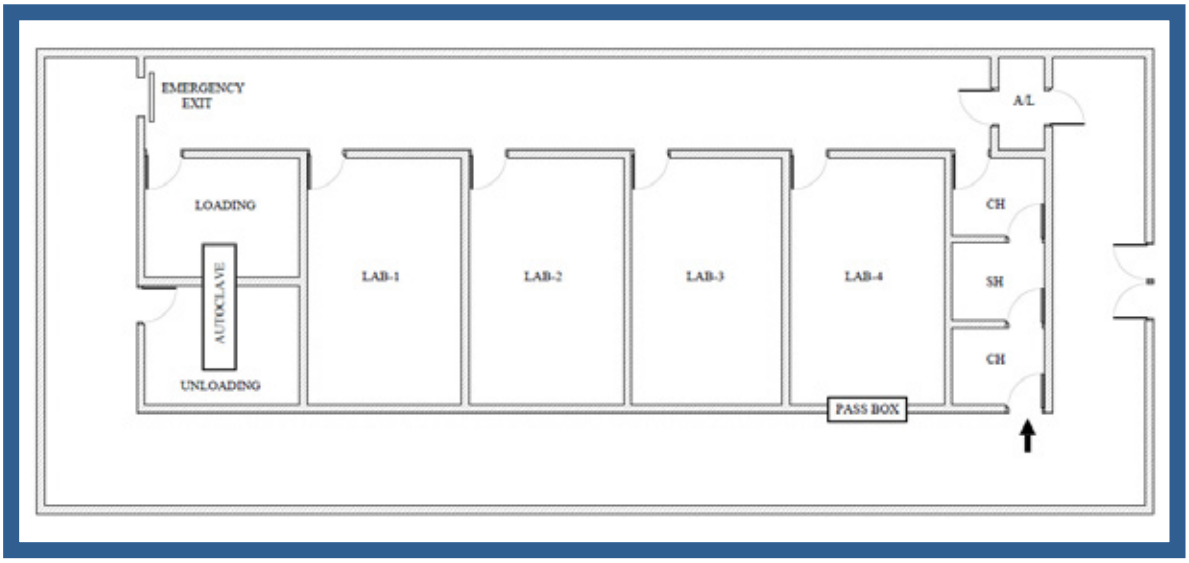
MODEL 4



Legend:

CH: Changing Room
SH: Shower
LAB-1: Animal Side
LAB-2: Lab Side
PB: PassBox
A/L: Airlock

MODEL 5



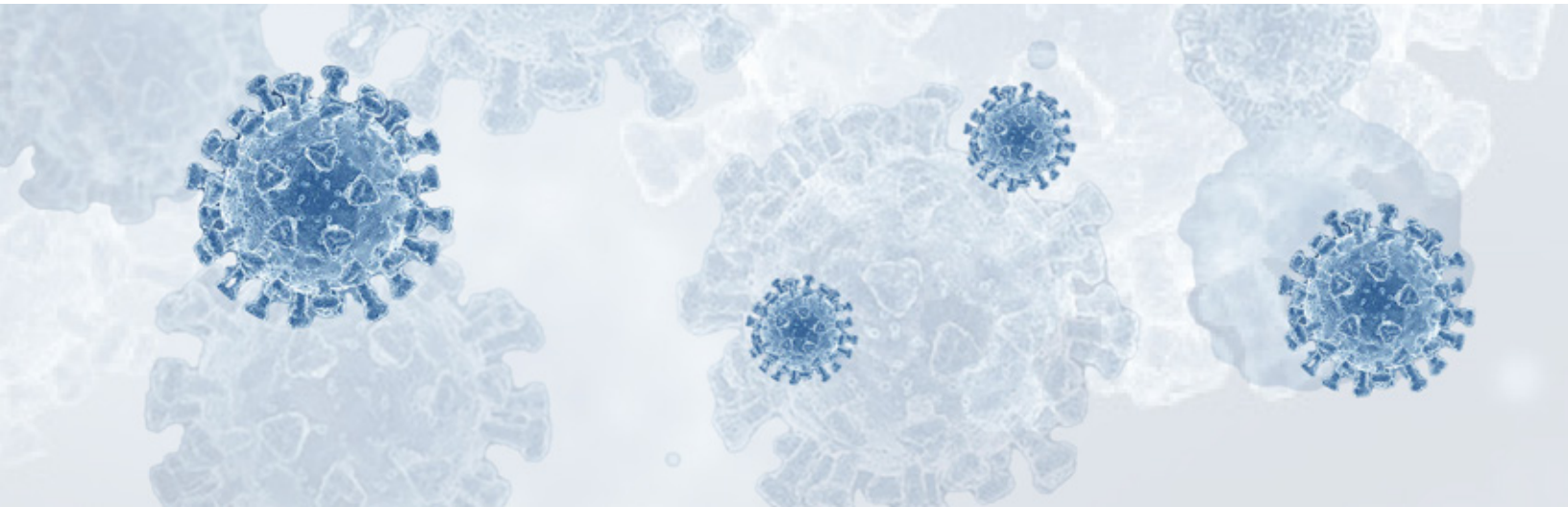
Legend:

CH: Changing Room
SH: Shower
PB: PassBox
A/L: Airlock

GLOSSARY

Biohazardous waste	Any waste containing infectious materials or potentially infectious substances.
Biosafety	The maintenance of safe conditions in biological research to prevent harm to workers, non-laboratory organisms and the environment.
Biosafety cabinet (BSC)	An enclosed, ventilated laboratory workspace for safely working with materials contaminated with (or potentially contaminated with) pathogens requiring a defined biosafety level.
Biosafety level (BSL)	A safety or Pathogen/Protection level, is a set of biocontainment precautions required to isolate dangerous biological agents in an enclosed laboratory facility.
Competent authority	An authority responsible for the implementation and application of health measures.
Containment	Safe methods (Combination of facilities, practices and procedures) for managing hazardous microorganisms, genetically engineered organisms or cells in the laboratory environment where they are being handled or maintained.
Contamination	The unintentional presence of an infectious organism on a human or animal body surface, instruments, product, parcels etc that may raise issues related to public health.
Disease	An illness due to a specific infectious organism or its toxic products that arises through transmission of that organism or its products from an infected person, animal or reservoir to a susceptible host, either directly or indirectly through an intermediate plant or animal host, vector or the inanimate environment
Decontamination	A procedure whereby health measures are taken to eliminate an infectious organism or toxic chemical agents.
Disinfection	A process that eliminates all pathogenic microorganisms, with the exception of bacterial spores, from inanimate objects, for the purpose of minimizing risk of infection.
Dual use items	Dual-use items refer to goods, technology, chemicals, organisms etc. which potentially have both, civil as well as military applications and are capable of being deployed as weapons of mass destruction.
Hazardous microorganisms	These are risk inherent microorganisms that may cause harm or likely to cause harm to public health and environment.

Health hazard	A factor or exposure that may adversely affect the health of a human population.
Health measure	Procedures applied to prevent the spread of disease or contamination; a health measure does not include law enforcement or security measures.
Infective microorganism	Infective microorganisms are those that could get access and colonize on human, animal. It may or may not cause disease.
Infection	The entry and development or multiplication of an infectious organism in the body of humans and animals that may constitute a public health risk.
Pathogen	Organism that infects and could cause disease. Pathogens exhibit different degree of virulence trait (the ability to cause host cell damage) and so vary in pathogenicity (ability to cause disease).
Personal Protective Equipment	Specialized clothing and equipment designed to create a barrier against health and safety hazards; examples include eye protection (e.g., goggles or face shields), gloves, surgical masks and particulate respirators.
Public health	The science and art of preventing disease, prolonging life and promoting health through organized efforts of society. It is a combination of sciences, skills, and beliefs that is directed to the maintenance and improvement of the health of all people through collective or social actions. The goals are to reduce the amount of disease, premature death and disease produced discomfort and disability in the population.
Risk	A situation in which there is a probability that the use of, or exposure to an organism or contaminated product will cause adverse health consequences or death.
Risk assessment	The qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards.
Risk Groups	Classifications that describe the relative hazard posed by infectious agents or toxins in the laboratory.
Three-tier security system	Security system, with three tiers, each tier representing access point, for example: External/Guard House barrier, Building/Lobby Restricted Entrance, and Restricted access to the containment facility/zone.



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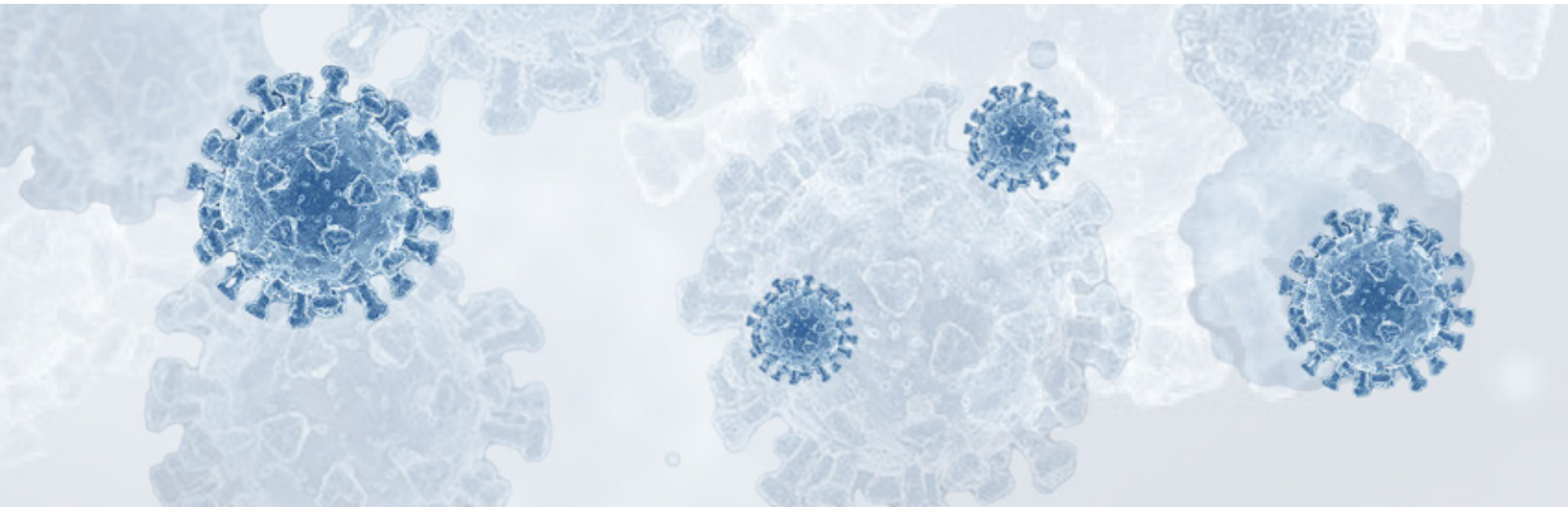

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  - Dr. Nitin Kumar Jain, Scientist G and Head, Regulation, DBT, New Delhi
  - Dr. Ashwin Raut, Principal Scientist, NIHSAD, Bhopal
  - Dr. Rahul Dhodapkar, Professor, JIPMER, Puducherry
  - Dr. Shashank Tripathi, Assistant Professor & Viral BSL-3 In-charge, IISC, Bangalore
  - Er. B. Vijayakumar, Executive Engineer, CSIR-CCMB, Hyderabad
  - Er. K.K. Gupta, Chief Technology Officer (Retd), NRCE, Hisar
  - Er. Ajay Khare, Sr. Technical Officer-3, ICMR-NIV, Pune
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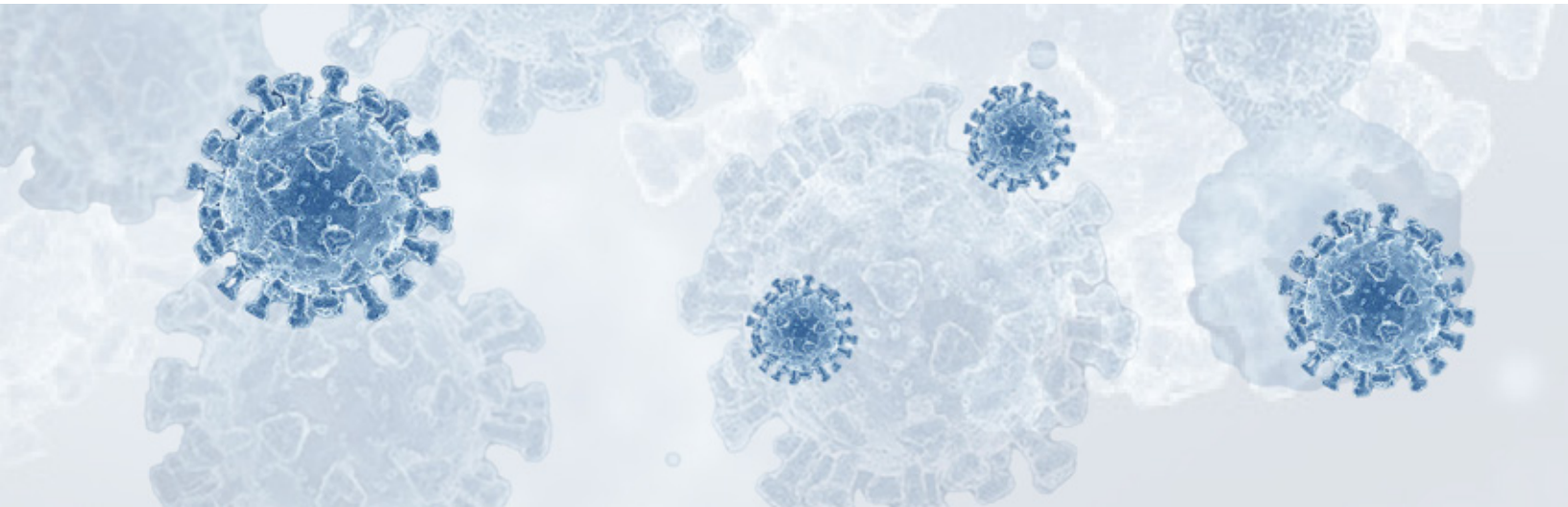
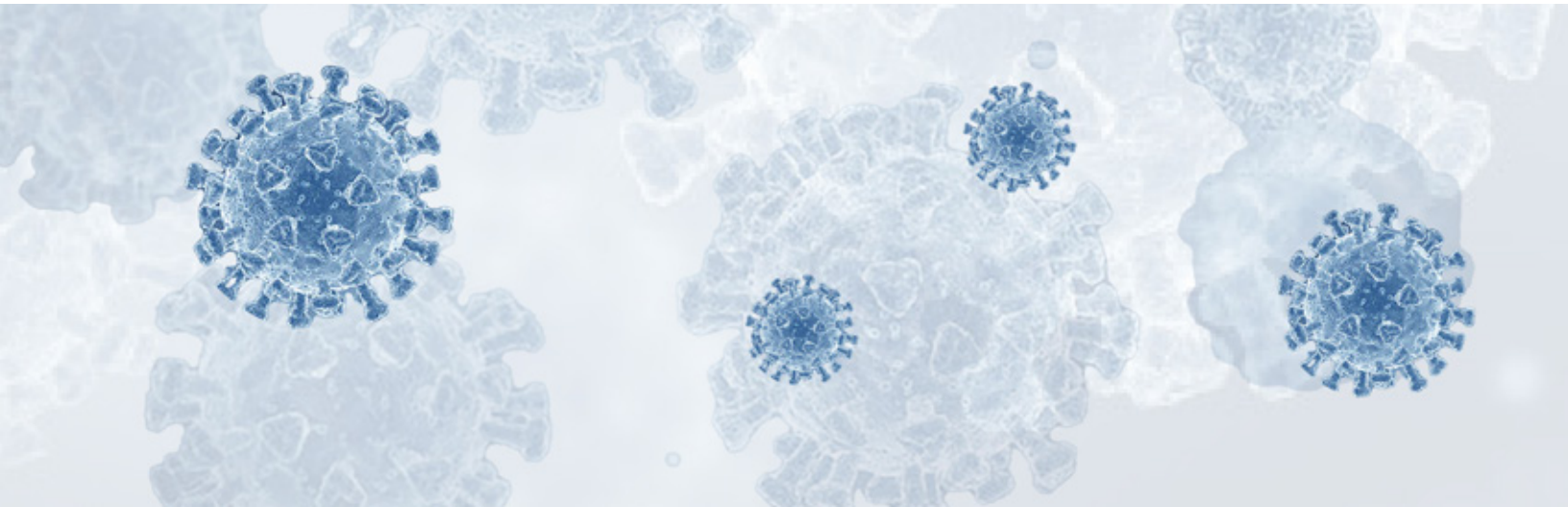
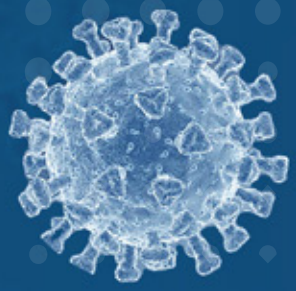


Department of Biotechnology
Ministry of Science and Technology
Government of India
Block 2, CGO Complex, Lodhi Road,
New Delhi - 110003, Delhi, India

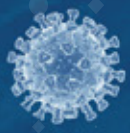
&

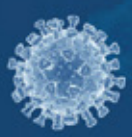
Indian Council of Medical Research
Ministry of Health & Family Welfare
Government of India
V. Ramalingaswami Bhawan,
Ansari Nagar,
New Delhi - 110029, Delhi, India





Frequently Asked Questions





FREQUENTLY ASKED QUESTIONS

1 What is biosafety?

- Biosafety refers to policies and procedures adopted to reduce/ minimize the risk to human health and to ensure environmental conservation.

2 What are the biosafety levels?

- "Biosafety Levels" (BSLs) are designations applied to projects or activities conducted in laboratories in ascending order of containment based on the severity of the health-related risk associated with the work being conducted. The designations include BSL-1, BSL-2, BSL-3, and BSL-4, describing the minimum safe work practices, specially designed buildings, and safety equipment required to conduct work on infectious agents, toxins, and other biological hazards. The BSL-4 is the highest biosafety level.

3 What is biocontainment?

- Biocontainment is a combination of facility design features and operating procedures to ensure that biohazards within a laboratory are not released into the outside environment.

4 What is a biological risk assessment?

- A biological risk assessment is a process that evaluates multiple factors to determine the risk to laboratory workers, the community, or the environment of working with an infectious agent, toxin, or other biological hazard. The biological risk assessment is used to determine the appropriate biosafety level for each project conducted within a laboratory.

5 How to determine if the microorganism is a BSL-3 pathogen?

- Biosafety levels are determined by the risk group classification for the organism and procedures used during experimentation. Please refer to "*List of infective Microorganisms corresponding to different Risk Groups",* as updated time to time and available on IBKP *(https://ibkp.dbtindia.gov.in/Content/Rules),* to see the risk group classification for a microorganism. Further, for working with organisms not listed here, investigators should determine the appropriate containment level in consultation with Institutional Biosafety Committee (IBSC).

6 What regulatory permissions need to be sought before initiating work involving pathogenic microorganisms?

- For regulatory permissions required to use pathogenic microorganisms for research and development, please refer to "*Regulations & Guidelines for Recombinant DNA Research and Biocontainment",* as updated time to time and available on IBKP *(https://ibkp.dbtindia.gov.in/Content/Rules).*

7 What type of approval is required while undertaking research and development work on RG-3 microorganisms?

- All category III and above GE experiments, requiring BSL-3 containment facility, require prior authorization from IBSC and subsequent approval from RCGM before commencement of the experiments through submission of information in the prescribed proforma (Form C1).

8 What is Institutional Biosafety Committees (IBSC)?

- Institutional Biosafety Committees (IBSCs) need to be constituted by all institutions handling hazardous microorganisms and/ or GE organisms. The Committee will be the nodal point for the implementation of the biosafety guidelines and for the interactions within the institution. For more details, please refer to *"Handbook for Institutional Biosafety Committees (IBSCs)"*, as updated time to time and available on IBKP *(https://ibkp.dbtindia.gov.in/Content/Rules)*.

9 How can an institution constitute an IBSC?

- Constitution of an IBSC and its registration in the Department of Biotechnology (DBT) through the Indian Biosafety Knowledge Portal (IBKP) is mandatory in India for every Applicant Agency undertaking R&D activities using GE organisms/ cells and hazardous microorganisms in accordance with the Rules 1989 of the EPA, 1986. For details, please refer to *"Handbook for Institutional Biosafety Committees (IBSCs)"*, as updated time to time and available on IBKP *(https://ibkp.dbtindia.gov.in/Content/Rules)*.

10 What are the functions of Review Committee on Genetic Manipulation (RCGM)?

- Review Committee on Genetic Manipulation (RCGM) functions in the Department of Biotechnology to monitor the safety-related aspect in respect of ongoing research projects or activities involving hazardous microorganisms, GE organisms and cells and products thereof. RCGM brings out Manuals of guidelines specifying procedure for regulatory process with respect to activities involving GE organisms in research use as well as industrial & environmental applications with a view to ensure human health and environmental safety. All ongoing research projects involving hazardous microorganisms, GE organisms or cells and products thereof are reviewed to ensure that adequate precautions and containment conditions are being met. RCGM lays down procedures restricting or prohibiting production, sale, importation and use of such hazardous microorganisms, GE organisms or cells.

11 What is a Biosafety Level 3 (BSL-3) containment facility?

- Biosafety Level 3 (BSL-3) is a containment facility applicable to clinical, diagnostic, teaching, research, or production facilities where work is performed with indigenous or exotic agents that may cause serious or potentially lethal disease through direct contact, fomites or inhalation route of exposure.

12 Who should establish a Biosafety Level 3 (BSL-3) containment facility?

- A BSL-3 containment facility may be established to facilitate research and diagnostic activities for new, emerging and re-emerging infectious pathogens that may cause potentially lethal disease in humans and animals, and to support avenues for drug discovery, diagnosis, and vaccines/therapeutics development. Accordingly, the decision to establish a BSL-3 facility should be based on the scope of the work to be carried out in the envisaged BSL-3 facility, with clearly identified and defined objectives. Further, all the activities involving handling of infectious agents should be performed as per the pre-defined laboratory-specific SOPs. Sufficient utilization of such a facility should be ensured, considering the high cost of establishment and maintenance.

13 What is the cost of establishment and maintenance of a Biosafety Level 3 (BSL-3) containment facility?

- A 1000 sq. ft. BSL-3 containment facility requires approximately 5-7 crores INR for its establishment and approximately 80 lakhs INR for annual maintenance.

14 What are the important considerations for the Construction of the BSL-3 facility?

- The BSL-3 facility has special engineering and design features. The technical standards for the engineering controls with respect to special safety practices, equipment, and facility requirements need to be considered prior to construction of the BSL-3 facility.

15 What is meant by the Commissioning of the containment facility?

- Commissioning is the verification of physical construction with the design parameters/ predetermined performance criteria, and it is an integral part of the overall validation process. This requires verification and documentation of critical containment components, equipment start-up, adjustments of parameters, control system calibration, balancing and performance testing.

16 What is meant by the Validation of the containment facility?

- Validation represents the successful completion of commissioning and acceptance of operational protocols that meet the required design parameters as per these guidelines. The validation of the containment facility is a documented process, which serves not only to verify the proper functioning of all four controls (Administrative, Engineering, Workplace practices and Personal protective equipment) during normal operation but also to ensure biosafety and biosecurity in the event of a failure of any of these controls.

17 Who will conduct the Validation of the containment facility?

- Validation of the BSL-3 facility should be conducted by qualified and competent ISO/IEC 17025 accredited organizations in the presence of

a third party (Expert Committee comprising of Scientists experienced in working/establishing BSL-3 laboratory, Engineers experienced in establishing/maintaining BSL-3 laboratory and representative of CPCB).

18 What is ISO/IEC 17025 accreditation?

- ISO/IEC 17025 accreditation is based on standards entitled "General Requirements for the Competence of Testing and Calibration Laboratories", published by the International Organization for Standardization (ISO), Geneva, Switzerland.

19 How to obtain information on ISO/IEC 17025 accredited organizations?

- In India, the National Accreditation Board for Testing and Calibration Laboratories (NABL) grants accreditation to Calibration Laboratories in accordance with ISO/IEC 17025 "General Requirements for the Competence of Testing and Calibration Laboratories". Please refer to their website for details of ISO/IEC 17025 accredited organizations *(https://nablwp.qci.org.in/laboratorysearchone)*. UK Certification and Inspection Ltd., London, United Kingdom *(www.ukcertifications.org.uk)*, may also be referred.

20 Why to seek certification of BSL-3 facility?

- In India, all activities related to Genetically Engineered organisms (GE organisms) or cells and hazardous microorganisms and products thereof are regulated as per the "Manufacture, Use/Import/Export and Storage of Hazardous Microorganisms/ Genetically Engineered Organisms or Cells, Rules, 1989" (Rules, 1989) notified by the Ministry of Environment, Forest and Climate Change (MoEF&CC), Government of India, under the Environment (Protection) Act, 1986 (EPA 1986).
- As per the provisions of Rules, 1989, RCGM, DBT has notified the *"National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024",* vide OM Dated 27.09.2024. With this notification, Certification of BSL-3 Laboratories shall be mandatory for all public and private organizations handling GE organisms and high-risk group pathogens for research, development and diagnostics support services.
- Further, DBT nominees of IBSCs to ensure that handling of GE organisms and high-risk group pathogens should not be initiated till certification of BSL-3 facilities by the respective Line Ministry.

21 How to seek certification for the BSL-3 facility?

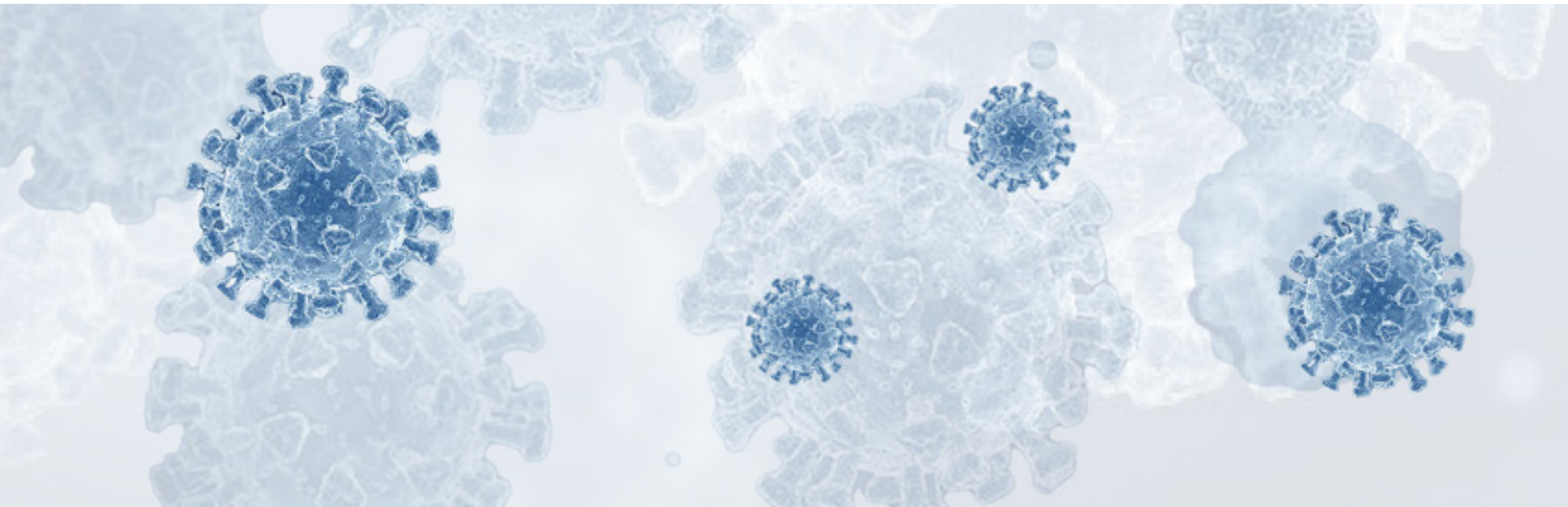
- All public and private organizations involved in handling of GE organisms and high-risk group pathogens for research, development and diagnostics support services need to comply with the *"National Guidelines for the establishment and certification of Biosafety Level-3 (BSL-3) Containment Facility, 2024"* and submit the application for Certification of BSL-3 Facility, as per the process mentioned in the guidelines.

22 What are the norms for Biomedical waste decontamination and disposal?

- The decontamination and disposal procedures mentioned in the *"Regulations and Guidelines on Biosafety of Recombinant DNA Research & Biocontainment"*, as updated time to time and available on IBKP, should be strictly complied with. A Memorandum of Understanding (MOU) along with valid Consent to Operate (CTO) with State Pollution Control Boards (SPCBs)/Pollution Control Committees (PCCs), as applicable, for compliance towards Biomedical waste decontamination and disposal, should be in place.

23 Are Emergency/Incident Procedures required?

- Emergency contingency plans shall be prepared, considering every possible breach in biocontainment, for each laboratory as well as for the institution. Any unforeseen incident/breach in containment must be immediately reported to the regulatory authorities. The Laboratory In-charge and Biosafety Officer, IBSC must be instantly notified. The IBSC must bring such incidents to the notice of RCGM/ GEAC. All such instances need to be duly recorded and reported.



Notes