National Department of Health

Title: LABORATORY BIOSAFETY MANUAL

ID: G_10_EX_001_A

Developed by:	**WHO 2020**
Reviewed by:	**J Ferguson**
Authorized by:	**W Porau**
Issued date:	**9/8/21**
Review period:	**2 years**

Abridged from WHO Laboratory Biosafety Manual 4th Edition

Original - https://www.who.int/publications-detail-redirect/9789240011311

Certification of printed copy:

Version	
Authorised by (name)	
Signed	
Date	

Contents

Section 1. Introduction

Laboratory biosafety and biosecurity activities are fundamental to protecting the laboratory workforce and the wider community against unintentional exposures or releases of pathogenic biological agents. These activities are implemented using a risk assessment framework and through the development of a safety culture which is needed to ensure a safe workplace where adequate measures are applied to minimize the likelihood and severity of any potential exposure to biological agents.

A review of recent laboratory-associated infections showed that most were caused by human factors rather than malfunctions of engineering controls *(4,5)*. Factors that have led to potential and confirmed exposures to biological agents include an absence or improper use of personal protective equipment (PPE) *(6,7)*, inadequate or ignored risk assessments *(8)*, lack of standard operating procedures (SOPs) *(9)*, needlestick injuries *(10,11)* and/or insufficiently trained personnel *(12)*. It can be argued, therefore, that the best designed and most well engineered laboratory is only as good as its least competent worker.

1.1 Intended scope

This fourth edition of the WHO *Laboratory biosafety manual* (LBM4) adopts a risk- and evidence-based approach to biosafety rather than a prescriptive approach in order to ensure that laboratory facilities, safety equipment and work practices are locally relevant, proportionate and sustainable. Emphasis is placed on the importance of a "safety culture" that incorporates risk assessment, good microbiological practice and procedure (GMPP) and SOPs, appropriate introductory, refresher and mentoring training of personnel, and prompt reporting of incidents and accidents followed by appropriate investigation and corrective actions.

This publication provides guidance specifically for those who work with biological agents or in facilities where personnel may be exposed to potentially infectious substances that present a hazard to human health. It can be used to drive a safety culture for every day laboratory practices and procedures. It will also be of value to those building or renovating laboratory facilities and to countries developing or implementing biosafety programs and national-level frameworks for biosafety oversight.

1.2 How to use this manual

This manual covers the following areas:

- risk assessment, control and review,
- core requirements for biosafety,
- options for heightened control measures,
- transfer and transportation of infectious substances,
- biosafety program management

Associated monographs have also been produced to provide more detailed information and help implement systems and strategies on specialized topics.

Section 2. Risk Assessment – abridged

For the complete section 2, refer to Laboratory biosafety manual, 4th edition (who.int) 2020.

As described in the sections below, the control of biological risks - whether at national or organizational levels - is informed by performing a risk assessment. Risk assessment is the term used to describe the stepwise process in which the risk(s) arising from working with a hazard(s) are evaluated and the resulting information is used to determine whether risk control measures can be applied to reduce those risks to acceptable risks. Risk is the combination of the probability that a hazard will cause harm and the severity of harm that may arise from contact with that hazard.

In the case of laboratory biosafety, the hazards are biological agents whose pathogenic characteristics give them the potential to cause harm to humans or animals should they be exposed to these agents. The harm caused by exposure to biological agents can vary in nature and can range from an infection or injury to a disease or outbreak in larger populations (see Box 2.1).

BOX 2.1 LIKELIHOOD AND CONSEQUENCE FOR LABORATORY BIOSAFETY

In the context of laboratory biosafety, likelihood refers to the potential for an exposure and/or a release outside of the laboratory. Consequence refers to the severity of the outcome from an exposure, if it were to occur. This could include a laboratory-associated infection, asymptomatic carriage, environmental contamination, spread of disease throughout the surrounding community or other illness or injury.

For this reason, factors that contribute to the occurrence of infection, such as routes of transmission, infectious dose and communicability, need to be considered in relation to the consequence of an exposure or release.

It is important to note that hazards alone do not pose a risk to humans or animals. For example, a vial of blood containing a biological agent such as Ebola virus does not pose a risk to the laboratory personnel until they come into contact with the blood contained within the vial. Therefore, the true risk associated with a biological agent cannot be determined by only identifying its pathogenic characteristics. Consideration must also be given to the types of procedure(s) that will be performed with the biological agent and the environment in which these procedures will take place. Any facility that handles biological agents has an obligation to their personnel and the community to perform a risk assessment on the work they will conduct and to select and apply appropriate risk control measures to reduce those risks to an acceptable risk. The purpose of the risk assessment is to gather information, evaluate it and use it to inform and justify the implementation of processes, procedures and technologies to control the risks present. Analysis of this information empowers laboratory personnel as it gives them a deeper understanding of the biological risks and the ways in which they can affect them. It helps create shared values, patterns of behaviour and perceptions of the importance of safety, and makes laboratory personnel more likely to conduct their work safely and maintain a safety culture in the laboratory.

Risk assessments must always be conducted in a standardized and systematic way to ensure they are repeatable and comparable in the same context. For this reason, many organizations offer risk assessment templates, checklists or questionnaires that provide stepwise approaches to identify, evaluate and determine risks associated with the hazards present, before using this information to identify appropriate risk control measures (24, 25). The various steps of the risk assessment process collectively form a risk assessment framework (Figure 2.1).

Figure 2.1 The risk assessment framework

Where Figure 2.1 illustrates the steps in the risk assessment framework, Table 2.1 provides an overview of the key considerations that apply during each step of the cycle. It is important to note that not all factors will affect risk in the same way, but each should be carefully considered. When conducting a risk assessment, it must be remembered that the risk is not based on the pathogenicity of the biological agent alone, but on the likelihood and consequence of an incident occurring – in other words, the risk of exposure to and/or release of the biological agent during laboratory operations.

Table 2.1 Key considerations in the risk assessment framework

STEP	KEY CONSIDERATIONS
1. Gather information (hazard identification)	▪ What biological agents will be handled and what are their pathogenic characteristics? ▪ What type of laboratory work and/or procedures will be conducted? ▪ What type(s) of equipment will be used? ▪ What type of laboratory facility is available? ▪ What human factors exist (for example, what is the level of competency of personnel)? ▪ What other factors exist that might affect laboratory operations (for example, legal, cultural, socioeconomic, public perception)?
2. Evaluate the risks	▪ How could an exposure and/or release occur? ▪ What is the likelihood of an exposure and/or release? ▪ What information gathered influences the likelihood the most? ▪ What are the consequences of an exposure and/or release? ▪ Which information/factor influences the consequences the most? ▪ What is the overall initial risk of the activities? ▪ What is an acceptable risk? ▪ Which risks are unacceptable? ▪ Can unacceptable risks be controlled, or should the work not proceed at all?

3. Develop a risk control strategy	▪ What resources are available for risk control measures? ▪ What risk control strategies are most applicable for the resources available? ▪ Are resources sufficient to obtain and maintain those risk control measures? ▪ Are proposed control strategies effective, sustainable and achievable in the local context?

Table 2.1 Key considerations in the risk assessment framework (continued)

STEP	KEY CONSIDERATIONS
4. Select and implement risk control measures	▪ Are there any national/international regulations requiring prescribed risk control measures? ▪ What risk control measures are locally available and sustainable? ▪ Are available risk control measures adequately efficient, or should multiple risk control measures be used in combination to enhance efficacy? ▪ Do selected risk control measures align with the risk control strategy? ▪ What is the residual risk after risk control measures have been applied and is it now acceptable? ▪ Are additional resources required and available for the implementation of risk control measures? ▪ Are the selected risk control measures compliant with national/international regulations? ▪ Has approval to conduct the work been granted? ▪ Have the risk control strategies been communicated to relevant personnel? ▪ Have necessary items been included in the budget and purchased? ▪ Are operational and maintenance procedures in place? ▪ Have personnel been appropriately trained?
5. Review risks and risk control measures	▪ Have there been any changes in activities, biological agents, personnel, equipment or facilities? ▪ Is there any new knowledge available of biological agents and/or the processes being used? ▪ Are there any lessons learnt from incident reports and investigations that may indicate improvements to be made? ▪ Has a periodic review cycle been established?

It should be noted that laboratories worldwide could face unique challenges that will influence how various parts of the risk assessment framework are conducted.

Challenges may include: the level of organizational and financial resources available to manage biological risks; absence of a reliable electrical supply; inadequate facility infrastructure; severe weather; under-staffed laboratories; and under-trained personnel. Furthermore, the status of national regulatory frameworks may influence the way in which risks are identified and controlled at a level higher than laboratory management, and compliance with any regulations should be a primary focus.

For these reasons, the results of a risk assessment and the risk control measures implemented may vary considerably from laboratory to laboratory, institution to institution, region to region and country to country.

Section 3. Core Requirements and Heightened Control Measures

The core requirements include a set of operational and physical elements that, when combined, should be sufficient to control the risks of most procedures with most biological agents in clinical and diagnostic laboratories. As previously mentioned, all the risk control measures implemented as part of the core requirements must be appropriately managed in order to help ensure a safe working environment, as described in section 7 biosafety program management.

Heightened control measures

For most procedures, the core requirements will be sufficient to keep risks acceptable. However, during the risk assessment, a situation may be identified in which the initial risk requires the use of one or more heightened control measures, over and above those outlined in the core requirements, to reduce the risks to acceptable risks.

3.1 Good microbiological practice and procedure (GMPP)

GMPP is a term given to a set of standard operating practices and procedures, or a code of practice, that is applicable to all types of activities with biological agents. This includes both general behaviours, best working practice and technical procedures that should always be observed in the laboratory and conducted in a standardized way. The implementation of standardized GMPP serves to protect laboratory personnel and the community from infection, prevent contamination of the environment, and provide product protection for the work with the biological agents in use.

GMPP are the most essential risk control measures because human error, suboptimal laboratory techniques and improper use of equipment have been found to cause the most laboratory injuries and laboratory-associated infections *(4,28-30)*.

It is essential that laboratory personnel are trained and proficient in GMPP to ensure safe working practices.

Heightened control measures

- PC2 Lab access controls required to allow only authorized staff and students to access the laboratory.
- BSC required for various specimen and culture manipulations including sputum sample microscopy, culture and GenXpert setup AND processing of positive blood cultures (Gram stain smears and subcultures)

3.2 Best practice

Best practice describes behaviours that are essential to facilitate safe work practices and control biological risks. Examples of laboratory best practice are outlined below.

- Never store food or drink, or personal items such as coats and bags in the laboratory. Activities such as eating, drinking, smoking, and applying cosmetics are only to be performed outside the laboratory.
- Never put materials, such as pens, pencils or gum, in the mouth while inside the laboratory, regardless of whether gloves are worn or not.
- Wash hands thoroughly, preferably with warm running water and soap, after handling biological material and/or animals, before leaving the laboratory or when hands are known or believed to be contaminated.
- Ensure open flames or heat sources are never placed near flammable supplies and are never

left unattended.
- Ensure that cuts or broken skin are covered before entering the laboratory.
- Before entering the laboratory, ensure that there are adequate supplies of laboratory equipment and consumables, including reagents, PPE and disinfectants, and that these items are suitable for the activities envisaged.
- Ensure that supplies are stored safely and according to storage instructions to reduce accidents and incidents such as spills, trips and falls.
- Ensure proper labelling of all biological agents and chemical and radioactive material.
- Protect written documents from contamination using barriers (such as plastic coverings), particularly those that may need to be removed from the laboratory.
- Ensure that the work is performed with care and without hurrying. Avoid working when fatigued.
- Keep the work area tidy, clean and free of non-essential objects and materials.
- Prohibit the use of earphones, which can distract personnel and prevent equipment or facility alarms from being heard.
- Cover or remove any jewelry that could tear gloves, easily become contaminated or become fomites. Cleaning and decontamination of jewelry or spectacles should be considered, if such items are worn regularly.
- Refrain from using portable electronic devices (for example, mobile telephones, tablets, laptops, flash drives, memory sticks, cameras, or other portable devices, including those used for DNA/RNA sequencing) when not specifically required for the laboratory procedures being performed.
- Keep portable electronic devices in areas where they cannot easily become contaminated or act as fomites that transmit infection. Where close proximity of such devices to biological agents is unavoidable, ensure the devices are either protected by a physical barrier or decontaminated before leaving the laboratory.

3.2.1 Technical procedures

Technical procedures are a special subset of GMPP which relate directly to controlling risks through safe conduct of laboratory techniques. These technical procedures, when executed correctly, allow work to be performed in a manner that minimizes the likelihood of cross contamination (that is contamination of other specimens, or previously sterile substances or objects as well as surface contamination) and also help prevent exposure of the laboratory personnel to biological agents. The following procedures help avoid certain biosafety incidents occurring.

Avoiding inhalation of biological agents

- Use good techniques to minimize the formation of aerosols and droplets when manipulating specimens. This includes refraining from forcibly expelling substances from pipette tips into liquids, over-vigorous mixing, and carelessly flipping open tubes. Where pipette tips are used for mixing, this must be done slowly and with care. Brief centrifuging of mixed tubes before opening can help move any liquid away from the cap.
- Avoid introducing loops or similar instruments directly into an open heat source (flame) as this can cause spatter of infectious material. Where possible, use disposable transfer loops, which do not need to be resterilized. Alternatively, an enclosed electric bactincerator to sterilize metal transfer loops can also be effective.

Avoiding ingestion of biological agents and contact with skin and eyes

- Wear disposable gloves at all times when handling specimens known or reasonably expected to contain biological agents. Disposable gloves must not be reused.
- Avoid contact of gloved hands with the face.
- Remove gloves aseptically after use and wash hands as outlined in Monograph: personal protective equipment (20).
- Shield or otherwise protect the mouth, eyes and face during any operation where splashes may

occur, such as during the mixing of disinfectant solutions.
- Secure hair to prevent contamination.
- Cover any broken skin with a suitable dressing.
- Prohibit pipetting by mouth.

Avoiding injection of biological agents

- Wherever possible, replace any glassware with plastic-ware.
- If required, use scissors with blunt or rounded ends rather than pointed ends.
- If glassware must be used, check it on a regular basis for integrity and discard it if anything is broken, cracked or chipped.
- Use ampoule openers for safe handling of ampoules.
- Minimize the risk associated with the use of syringes or needles by using blunt syringe needles, alternative devices or engineered sharp safety devices where possible. However, be aware that sharp safety devices also pose a risk when not handled properly.
- Never use syringes with needles as an alternative to pipetting devices.
- Never re-cap, clip or remove needles from disposable syringes.
- Dispose of any sharps materials (for example, needles, needles combined with syringes, blades, broken glass) in puncture-proof or puncture-resistant containers fitted with sealed covers. Disposal containers must be puncture-proof/-resistant, must not be filled to capacity (three-quarters full at most), must be never reused and must not be discarded in landfills.

Preventing dispersal of biological agents

- Discard specimens and cultures for disposal in leak-proof containers with tops appropriately secured before disposal in dedicated waste containers.
- Place waste containers, preferably unbreakable (such as plastic, metal), at every workstation.
- Regularly empty waste containers and securely dispose of waste.
- Ensure all waste is properly labelled.
- Consider opening tubes with disinfectant-soaked pad/gauze.
- Decontaminate work surfaces with a suitable disinfectant at the end of the work procedures and if any material is spilled.
- When disinfectants are used, ensure the disinfectant is active against the agents being handled and is left in contact with waste materials for the appropriate time, according to the disinfectant being used.

3.3 Personnel competence and training

Human error and poor technical skills can compromise the best safeguards. Thus, competent and safety-conscious laboratory personnel, who are well informed on how to recognize and control laboratory risks, are essential for the prevention of laboratory-associated infections and/or other incidents. Table 3.1 outlines the training that must be implemented for laboratory personnel.

An effective safety program begins with financial and administrative support from the laboratory management that enables and assures safe laboratory practices and procedures are integrated into the training of all personnel.

Measures to ensure that employees have read and understood the guidelines, such as signature pages, must be adopted. Laboratory supervisors have the main role in training their immediate personnel in GMPP.

Heightened control measures

Additional training will be required for any procedures, biological agents, systems or equipment that require heightened control measures.

Training should include both competency in the related protocols (including any maintenance, if required) and emergency operations should an incident occur, or the risk control measure fail.

A prescribed period of mentorship is recommended when using the heightened control measure and its associated procedures until personnel are considered competent.

Competence in the relevant procedure must be assessed and documented before unsupervised work proceeds. Competency must be regularly reviewed to ensure best practices are maintained.

Table 3.1 Training to be implemented for laboratory personnel

TRAINING	AREAS TO BE COVERED
General familiarization and awareness training	Mandatory for ALL personnel, an introduction to: ▪ Laboratory layout, features and equipment ▪ Laboratory code(s) of practice ▪ Applicable local guidelines ▪ Safety or operations manual(s) ▪ Institutional policies ▪ Local and overarching risk assessments ▪ Legislative obligations ▪ Emergency/incident response procedures
Job-specific training	▪ Training to be determined based on job function; training requirements may vary between personnel of the same job title but performing different functions ▪ All personnel involved in the handling of biological agents must be trained on GMPP ▪ Competency and proficiency assessment must be used to identify any other specific training required, for example, by observation and/or qualification ▪ Proficiency in any procedure must be verified before working independently, which may require a mentorship period ▪ Competencies must be reviewed regularly and refresher training undertaken ▪ Information on new procedures, equipment, technologies and knowledge must be communicated to applicable personnel as and when available
Safety and security training	Mandatory for ALL personnel: ▪ Awareness of hazards present in the laboratory and their associated risks ▪ Safe working procedures ▪ Security measures ▪ Emergency preparedness and response

GMPP = good microbiological practice and procedure.

3.4 Facility design

The facility design features listed below are core requirements for biosafety for all laboratories handling biological agents.

- 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 opening), appropriate fire ratings and 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 applies also 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 be provided outside the laboratory.
- Facilities for eating and drinking must be provided outside 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.
- Emergency situations 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.

For further information and an expansion of these core laboratory requirements and recommendations, refer to *Monograph: laboratory design and maintenance (21)*.

Heightened control measures

PC2 facility design requirements for microbiology sections in are described in the following document: Physical Containment 2 (PC2) Standard Lab Requirements G_10_Info_2_A

3.5 Specimen receipt and storage

Safe handling of biological agents begins even before a specimen arrives in the laboratory. When not properly packaged, infectious substances received in the laboratory can pose a safety risk to personnel. The following subsections describe the risk control measures that should be in place when receiving, storing and inactivating specimens as part of the core requirements for biosafety. For more information on the control requirements for handling biological agents before they reach the laboratory (that is while in transit), please refer to section 6 transfer and transport.

3.5.1 Receiving specimens

A specimen received by the laboratory must be accompanied by sufficient information to identify what it is, when and where it was taken or prepared, and which tests and/or procedures (if any) are to be performed.

Personnel unpacking and receiving specimens must be adequately trained in:

- awareness of the hazards involved,
- how to adopt necessary precautions according to GMPP described above,
- how to handle broken or leaking containers to prevent exposure to biological agents, and
- how to handle spills and use disinfectants to manage any contamination.

Specimens must be observed on receipt to make sure they have been packaged correctly according to shipping requirements and that they are intact. Where breaches of packaging are observed, the package should be placed in an appropriate sealable container. This surface of the container should then be decontaminated and transferred to an appropriate location such as a BSC before opening. The breach in packaging should be reported to the sender and couriers.

Specimen request or specification forms must be placed separately, preferably in waterproof envelopes, away from potential damage or contamination. Laboratories that receive large numbers of specimens should consider designating a room or area specifically for receiving specimens.

3.5.2 Storing specimens

Specimens must be stored in containers that are:

- made of adequate strength, integrity and volume to contain the specimen,
- leak-proof when the cap or stopper is correctly applied,
- made of plastic (whenever possible),
- free of any biological material on the outside of the packaging,
- correctly labelled, marked and recorded to facilitate identification, and
- made of an appropriate material for the type of storage required.

Care must be taken when storing specimens in liquid/vapour phase nitrogen.
Only tubes specifically noted by the manufacturer as being suitable for liquid nitrogen cryogenic storage should be used to reduce the likelihood of breakage on removal from liquid nitrogen. It is important to note that liquid and vapour can enter improperly sealed or cracked tubes and can rapidly expand on removal of the tube from storage; this can lead to breakage and/or explosion. Thermal

protective gloves and apron should be worn when accessing liquid nitrogen storage and a visor should be worn for splash protection.

3.5.3 Inactivating specimens

Inactivation methods must be appropriately validated whenever an inactivation step is used upon receipt of specimens or before transferring the specimens to other areas for further manipulation, such as PCR analysis or AFB smear examination. More information on inactivation can be found in *Monograph: decontamination and waste management (22)*.

Heightened control measures

- AFB smears to be heat fixed prior to staining
- Opening specimens (from their transfer or transport containers) within a primary containment device and/or while wearing additional PPE.
- Developing additional internal transfer and transport mechanisms.

3.6 Decontamination and waste management

Any surface or material known to be, or could potentially be, contaminated by biological agents during laboratory operations must be correctly managed to control biological risks. Core biosafety requirements for the handling of contaminated
waste material require that processes for the identification and segregation of contaminated materials be adopted before decontamination and/or disposal.
Where decontamination cannot be performed in the laboratory area or onsite, the contaminated waste must be packaged in an approved (that is leak-proof) manner for transfer to another facility with decontamination capacity. For more information on this process, please refer to section 6 transfer and transport.

A summary of different categories for segregating laboratory waste and their recommended treatment is given in Table 3.2.

Table 3.2 Categories of segregated laboratory waste materials and their recommended treatment

CATEGORY OF LABORATORY WASTE MATERIAL	TREATMENT
Uncontaminated (non-infectious) material	Can be reused or recycled or disposed of as general municipal waste
Contaminated sharps (hypodermic needles, scalpels, knives and broken glass)	Must be collected in puncture-proof containers fitted with covers and treated as infectious
Contaminated material for reuse or recycling	Must be first decontaminated (chemically or physically) and then washed; thereafter it can be treated as uncontaminated (non-infectious) material
Contaminated material for disposal	Must be decontaminated onsite OR stored safely before transportation to another site for decontamination and disposal
Contaminated material for incineration	Must be incinerated onsite OR stored safely before transportation to another site for incineration
Liquid waste (including potentially contaminated liquids) for disposal in the sanitary sewer system	Should be decontaminated before disposal in the sanitary sewer

The eventual treatment of the segregated waste will depend on the type of material, the biological agent(s) being handled, locally available decontamination methods and locally available protocols for decontamination. Additional consideration of non- biological hazards, for example, chemicals or sharps, may be required to ensure that risk control measures are in place to minimize these non-biological risks.

Where decontamination treatments are applied to surfaces and/or materials, the method must have been validated for the specific biological agents used and must be compatible with the materials and equipment being treated to avoid corrosion or damage. Proof of efficacy and efficiency of the method should be able to be produced to validate that the contaminated waste has been effectively decontaminated.

The following subsections describe some of the most common methods of decontamination used by laboratories and the core requirements to ensure their effective use to control biological risks. They include both chemical and physical decontamination methods. Detailed information can be found in Monograph: decontamination and waste management (22).

3.6.1 Chemical disinfection

Chemical disinfection is a method of decontamination that involves the application of a chemical, or mixture of chemicals, to an inanimate surface or material to inactivate viable biological agents or reduce their number to a safe level. Disinfectants are usually the preferred method for decontamination of surfaces; however, this is generally not required for regular cleaning of floors, walls, equipment and furniture as a core requirement for biosafety. Disinfectants should be used after a spill, or where contamination is known or suspected to have occurred. Disinfection of surfaces (and materials where applicable) should also be performed after work has been completed on the bench and periodically as part of a cleaning regime. Disinfectants can also be used for decontamination of contaminated liquids.

As there is an ever-increasing number and variety of commercial disinfectant products, formulations must be carefully selected for the specific needs of the laboratory based on the effectiveness of decontamination and compatibility with the equipment and materials.

Heavily soiled material may require pre-cleaning (that is the removal of dirt, organic matter and stains) before decontamination as many disinfectants claim to be active only on pre-cleaned items. Pre-cleaning must be performed with care to avoid exposure to and further spread of biological agents.

In choosing the disinfectant, three important factors must be considered for optimum effectiveness against biological risks:

- spectrum of laboratory activity (with high specificity for the biological agents to be disinfected),
- field of application (for example, application in liquids or on surfaces), and
- application conditions (contact time, concentration of the disinfectant, temperature of the application and other important influencing factors such as the presence of an organic load, for example, serum or blood).

Non-biological hazards posed by chemical disinfectants should also be considered and appropriate non-biological risk control measures applied. For example, many chemical disinfectants may be harmful to humans, animals and/or the environment or pose a fire or explosion risk. For this reason, chemical disinfectants must be selected, stored, handled, used and disposed of with care, following manufacturers' instructions. Particular care is needed in the use and storage of such chemicals in

tropical regions where their shelf life may be reduced because of high ambient temperatures and exposure to sunlight. PPE should be used to reduce the likelihood of exposure of personnel to both the chemical hazard and any biological agents present. Specific guidance on PPE requirements can be found in safety data sheets (also called material safety data sheets) provided by the manufacturer. Detailed information on the use of chemical disinfectants can be found in *Monograph: decontamination and waste management (22)*.

3.1.1 Autoclaving

Autoclaving, when used correctly, is the most effective and reliable means to sterilize laboratory materials and decontaminate waste materials by destroying or inactivating biological agents.

Autoclaving uses high temperatures (for example, 121 °C, 134 °C) applied as moist heat (steam) under pressure to destroy microorganisms. Achieving sufficiently high temperature is required because, although most infectious biological agents are destroyed by heating at 100 °C, some are heat-resistant (such as spores) that cannot be destroyed at this temperature. Autoclaving allows a higher temperature and
pressure to be achieved and maintained for a period of time that is sufficient for spore inactivation.

Different types of waste materials generally require different operating cycles to achieve appropriate inactivation temperatures. Therefore, laboratory autoclaves should be selected based on defined criteria such as intended use, and type and amount of waste to be decontaminated. Their effectiveness for the specific cycles that will be used should then be validated.

The main component of an autoclave is a pressure vessel (or sterilization chamber), which can be sealed tightly by a lid or a door. An arrangement of pipes and valves allows steam to be introduced and removed.

In simple devices (Figure 3.1), the lower part of the vessel is filled with water, which can then be evaporated by an electric heater. Steam produced at the beginning of the process displaces air in the chamber, which exits through an exhaust valve.

The holding time, temperature and pressure used for the autoclave cycle help determine the efficiency of inactivation. Autoclaves must therefore be equipped with systems to check these parameters. A written log should be maintained to record, for each cycle performed, the time, date, operator name, and type and approximate amount of waste that was treated.

Since air is an efficient insulator, it is essential that air is effectively removed from the chamber in order to ensure temperatures are not affected. Air displacement and removal can be supported and accelerated by a prevacuum process with repeated steam injection and evacuation steps. This is particularly important in the case of porous loads, from which it is difficult to displace the air. It is essential that the material is packed in an air- and vapour-permeable way to allow complete removal of the air. Air pockets trapped inside the goods prevent proper steam contact, lead to cold spots and may prevent complete inactivation of biological agents. The criteria for loading the autoclave chamber must therefore be precisely defined so that complete air evacuation and steam penetration are always guaranteed, even under worst-case conditions.

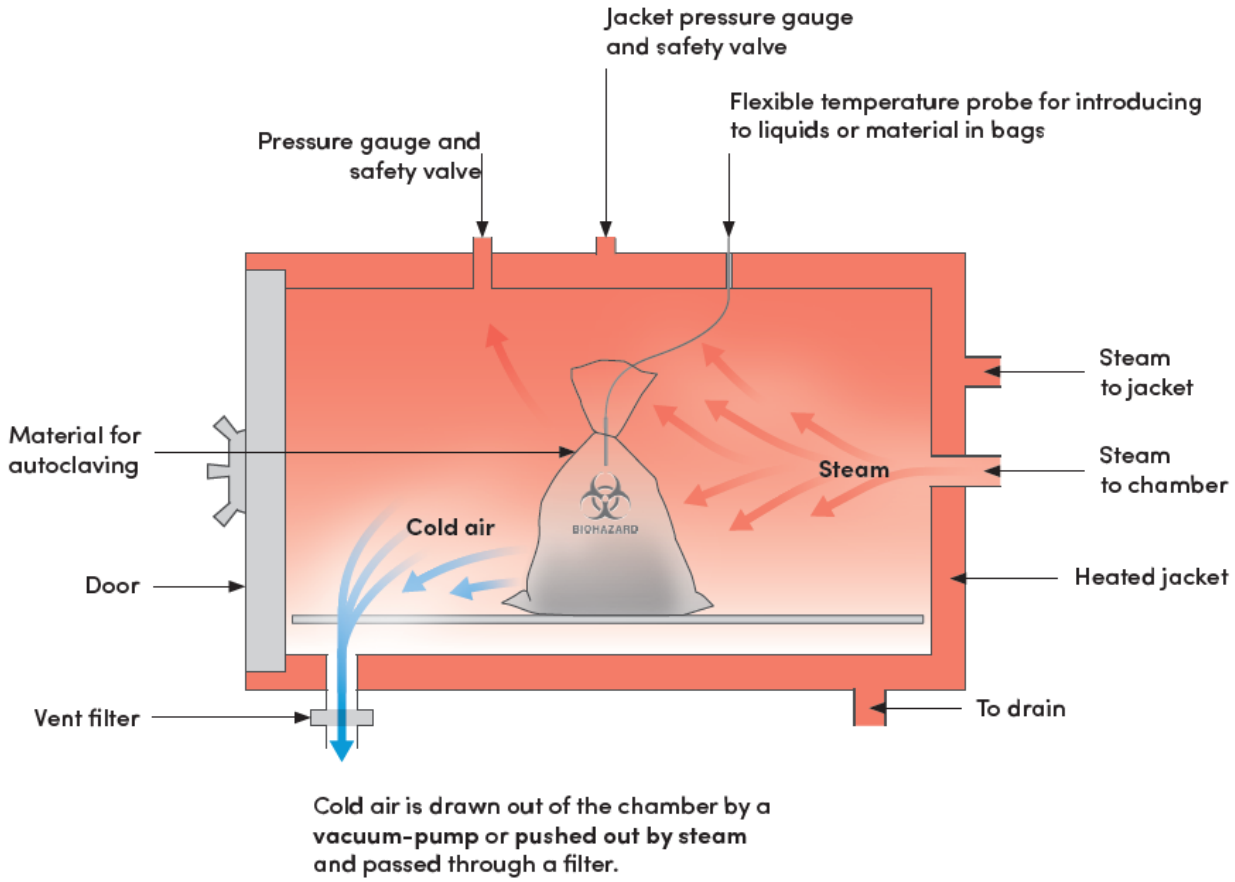

Figure 3.1 Simple laboratory autoclave

Autoclave operation

There are autoclave cycles operating with a vacuum (active) or without vacuum (passive).

Active (vacuum pump): the chamber is subjected to successive pressure changes to draw air from the chamber (vacuum–steam) through a vent filter (based on a risk assessment).

This is required for loads such as waste bags, glassware and other equipment where trapped air cannot reliably be removed by passive methods. The more difficult air is to remove, the more pressure pulses will be required.

Passive: steam enters the chamber and cold air is pushed out by the steam. This is the simpler method, but is only suitable for loads which do not impede the removal of air from the chamber.

The proper inactivation of contaminated waste must be regularly checked. In addition to temperature, pressure and time monitored by the autoclave, biological indicators should also be used periodically to prove inactivation. Because of its heat-resistant characteristics, spores of *Geobacillus sterothermophilus* are most often used for efficiency testing. These biological indicators are designed to demonstrate that an autoclave is capable of destroying microorganisms. Alternatively, the biological agents used in the laboratory can also serve as biological indicators for waste inactivation.

There are also different classes of chemical indicators available, from simple indicators to multiparameter indicators, which provide more accurate checks of time and temperature. These test strips usually show a characteristic and recognizable colour change, but this does not necessarily prove that the waste has been completely inactivated. It only indicates that the product has undergone certain treatment conditions defined by the manufacturer. A simple chemical indicator or autoclave tape can be used as a visual control to avoid confusion between treated and untreated material. However, these indicators do not provide any information on how long a certain temperature has been

maintained or whether inactivation was successful.

More information on the types and use of indicators for the performance testing of an autoclave, can be found in Monograph: decontamination and waste management (22).

The following general safety precautions must be taken when using steam autoclaves.

- Operation and maintenance of autoclaves must be assigned to trained, competent individuals.
- Operating instructions for the autoclave must be available. Sterilization programs with application area (for example, solids, liquids) and the parameters to be maintained (temperature, pressure, time) must be defined.
- A loading plan (with information on the contents, number, volume and mass of the sterilized product) should also be available. Large and bulky material, large animal carcasses, sealed heat-resistant containers and other waste that impedes the transfer of heat must be avoided.
- A preventive maintenance program must be developed, including regular visual inspection of the chamber, door seals, gauges and controls. This should be conducted by qualified personnel.
- A reliable steam source must be used to provide appropriately saturated steam, uncontaminated by water droplets or chemicals which inhibit the function of the autoclave, or may damage the pipes or chamber of the autoclave.
- Waste or materials placed in the autoclave must be in containers that readily allow removal of air and permit good heat penetration.
- The chamber of the autoclave must be loosely packed so that steam can penetrate evenly.
- Hazardous chemical waste (for example, bleach), mercury or radioactive waste must not be treated in an autoclave.
- Operators must wear suitable thermally protective gloves, protective clothing and eye protection when opening the autoclave, even when the temperature has fallen to levels appropriate for opening the chamber.
- Care should be taken to ensure that the relief valves and drains of autoclaves do not become blocked by paper, plastic or other materials included in the waste or materials for decontamination.
- For the decontamination of volatile hazardous material (for example, spores of pathogens) the air relief of the autoclave must be equipped with an appropriate filter.

More information on the various types of autoclave and their validation, maintenance and specifications can be found in Monograph: decontamination and waste management (22).

3.6.2 Incineration

Alternative methods of decontamination can be used if disinfection cannot be achieved or validated because of the large size or increased bioburden of the contaminated materials. A commonly used inactivation method is incineration, which also acts as a disposal mechanism, including for animal carcasses.

Use of incineration must meet with the approval of local public health and air pollution authorities. Incinerators must be appropriate for use with the material being incinerated; for example, one normally used for the incineration of paper is not suitable for laboratory waste. A complete burn must be achieved, that is complete to ash.

This is particularly important if burn pits are being used, for example, in an emergency, to avoid the potential for infection. Emission of decomposition odours and attraction of vermin defeats the purpose of the exercise.

Heightened control measures (waste management)

Waste generated by procedures using should preferably be decontaminated onsite, or close to the laboratory, to minimize the risk of exposure or release during waste transportation.

Where onsite decontamination is not possible, solid waste must be appropriately packaged, stored (if required) and transferred as soon as possible to another facility with decontamination capabilities. Infectious waste must first comply with any applicable transportation regulations if it is to be removed from the laboratory for decontamination and disposal. Consideration should be given to transporting waste in sealed and leak-proof containers.

3.1 Personal protectiveequipment

PPE refers to a set of wearable equipment and/or clothing worn (for example, gloves) by personnel to provide an additional barrier between them and the biological agents being handled, which effectively controls risk by reducing the likelihood of exposure
to the agents. A selection of the most common PPE that must be used as a core
requirement for biosafety are described in the following subsections.

Any PPE used in the laboratory must be correctly fitted, and personnel must be given adequate training in order to ensure it is used properly and effectively. Incorrect use of PPE, for example, unfastened laboratory coats, will not give the protection they are designed to provide. When combinations of PPE are worn together, they must complement one another and continue to fit properly.

It is important to note that there is not one size, type and/or brand that is appropriate for all personnel. Laboratory personnel should be consulted and a selection of items tested in order to procure the most effective items. Compliance with wearing PPE will generally be improved when users have input on comfort and fit.

Detailed information on selection, validation, fit testing and other considerations for PPE can be found in *Monograph: personal protective equipment (20)*.

3.1.1 Laboratory coats

Laboratory coats must be used in laboratories to prevent personal clothing from getting splashed or contaminated by biological agents. Laboratory coats must have long sleeves, preferably with fitted cuffs, and must be worn closed. Sleeves should never be rolled up. Coats must be long enough to cover the knees, but not trail on the floor.

Where possible, the fabric of the laboratory coat should be splash-resistant and overlap at the front. Laboratory coats can be reusable or disposable, although where reusable coats are used laundering of the coats must be done by the laboratory or specialist contractor. Laundering must be done regularly, and consideration should be given to autoclaving any visibly contaminated coats before laundering.

Laboratory coats must only be worn in designated areas. When not in use, they should be stored appropriately; they should not be hung on top of other laboratory coats, or in lockers or hooks with personal items. Laboratory coats should not be taken home by personnel.

Heightened controls

Laboratory coats that overlap at the front must be used to provide extra protection against splashes and spills.

3.1.1 Footwear

Footwear must be worn in the laboratory and must be of a design that minimizes slips and trips and can reduce the likelihood of injury from falling objects and exposure to biological agents. Footwear should cover the top of the foot, and should be well-fitting and comfortable to allow personnel to perform their tasks without fatigue or distraction.

Heightened controls

For bacteriological media production units, footwear may need to be changed and/or covered before entry into the laboratory if there is a requirement to prevent cross contamination.

3.1.2 Gloves

Appropriate disposable gloves must be worn for all procedures that may involve planned or inadvertent contact with blood, body fluids and other potentially infectious materials. They must not be disinfected or reused as exposure to disinfectants and prolonged wear will reduce the integrity of the glove and decrease protection to the user. Gloves should always be inspected before use to check they are intact.

Different types of gloves may be needed for different applications or other occupational hazards, such as thermal protection, or protection from sharps or against chemicals.

Various sizes should be available to ensure that gloves properly fit the user to allow adequate movement and dexterity for the procedures being performed. Nitrile, vinyl and latex gloves are often used for protection against biological agents. It should be noted that latex protein could cause allergy over time; low protein and powder-free options are available to minimize the occurrence of an allergy.

3.1.3 Eyeprotection

Safety glasses, safety goggles, face shields (visors) or other protective devices must be worn whenever it is necessary to protect the eyes and face from splashes, impacting objects and artificial ultraviolet radiation. Eye protection must be cleaned after every use. If splashed, it must be decontaminated with an appropriate disinfectant.

Personal prescription glasses (spectacles) must not be used as a form of eye protection as they do not cover enough of the face around the eyes, particularly around the side of the head. Specialized prescription safety glasses must be purchased for personnel with such needs. Some goggles are available that have recesses that enable the user to wear glasses underneath them.

3.1.4 Respiratoryprotection

Respiratory protection is generally not required for protection against biological agents as a part of the core requirements. Where a risk assessment indicates that the use of respiratory protection is needed, this is considered a heightened control measure. However, there may be circumstances where respiratory protection is required for other reasons based on assessments for non-biological hazards such as chemicals or allergens.

3.7 Laboratory equipment

When used effectively together with GMPP, the safe use of laboratory equipment will help minimize the likelihood of exposure of personnel when handling or manipulating biological agents.

For equipment to effectively reduce risks, laboratory management must make sure sufficient space is

provided for its use. An appropriate budget must be available for the equipment's operation and maintenance, including equipment incorporated into the facility design, which should be accompanied by specifications that outline its safety features. All personnel operating or maintaining a piece of equipment must be properly trained and be able to demonstrate proficiency.

Records must be kept detailing equipment use, any maintenance performed, and any validation/calibration procedures undertaken and their results. Where appropriate, the following records should also be kept:

- equipment inventories (which may also include details on age, condition, functioning),
- equipment purchase requests,
- contact information of people authorized to purchase, install, calibrate, validate, certify, operate and maintain equipment,
- unscheduled maintenance or incidents, and
- training and proficiency of personnel authorized for equipment use.

Selected equipment must be designed, constructed and installed so that it facilitates simple operation and allows for maintenance, cleaning, decontamination and certification to be performed in a way that contact between the operators and biological agents is prevented or limited wherever possible. Equipment must be constructed of materials that are impermeable to liquids (including chemicals used for decontamination), resistant to corrosion and that meet the structural requirements of the required tasks. It should be built free of sharp edges and unguarded moving parts to prevent occupational hazards to personnel. Large laboratory equipment must be placed so that the workflow of laboratory personnel, specimens and waste is unobstructed. It must also be placed so that its performance will be unaffected; for example, autoclaves must be located in a well-ventilated area because of their inherent heat production. Frequently used laboratory equipment such as incubators, refrigerators, freezers and centrifuges must be located ergonomically for laboratory personnel so it is easily accessible to avoid over-reaching and/or to allow work to proceed without overcrowding, which can increase the risk of musculoskeletal injury.

Equipment must be judged fit for purpose before use, which will usually be outlined in the manufacturer's instructions. Unless laboratory SOPs indicate otherwise, the manufacturer's instructions must always be followed.

All equipment must be checked regularly for integrity and to identify potential faults. Any faults must be reported immediately and corrective actions taken to rectify them before the equipment is used again. Performance verification must be done at regular intervals, in between scheduled preventive maintenance and servicing, to ensure the equipment is functioning as expected.

3.6.3 Specialized laboratory equipment

Best practice is required when using some of the most commonly used pieces of laboratory equipment in order to effectively reduce biological risks. These types of equipment are described in the following subsections.

Pipettes

To prevent the generation of aerosols, pipettes must not be used to blow air or forcibly expel liquids/solutions that contain biological agents. All pipettes and/or the pipette tips should have cotton plugs to reduce contamination of pipetting devices.

As an important part of GMPP, all personnel must be adequately trained in the correct use of pipettes to reduce risks of contamination caused by aerosolization and splashing and thus improve both safety and quality.

To avoid further dispersion of any biological agents that might be dropped from a pipette tip, an absorbent material may be placed on the working surface and disposed of as infectious waste after use. Contaminated pipettes or tips can be completely submerged in a suitable disinfectant in an unbreakable container. If chemically disinfected, they should be left in the disinfectant for the appropriate length of time before disposal or washing. Pipette tips are normally autoclaved, but pipettes are unlikely to withstand the autoclaving process.

Centrifuges

All centrifuges must be operated and serviced according to manufacturers' instructions and serviced by appropriately qualified personnel. Where safety buckets are available for a centrifuge, these must be used. Sealing rings for buckets must be checked regularly for integrity and replaced if cracks appear.

When using centrifuges, the contents of centrifuge tubes must be filled to the same level and placed in the centrifuge at opposite locations to make sure the centrifuge is balanced during operation. Centrifuges must be cleaned and disinfected regularly, or immediately decontaminated after a spill, with an appropriate disinfectant.

Refrigerators and freezers

Refrigerators and freezers must be spark-proof if they are to store flammable solutions. Notices to this effect must be placed on the outside of the doors. Appropriate PPE must be worn when handling specimens from cryogenic storage, for example, thermal protective apron and gloves, as well as face and eye protection when placing specimens in or removing them from liquid nitrogen. All containers stored inside refrigerators and freezers must be clearly labelled so that they can be easily identified. An inventory of their contents must be maintained and controlled periodically.

Unlabelled materials must be assumed to be infectious and must be decontaminated and discarded using appropriate waste channels. Unlabelled items should also be reported as a near miss as this indicates a failure of the SOPs and risk assessment.

Heightened controls (equipment)

Special consideration may need to be given to the equipment being used during higher risk procedures. These include:

- applying additional containment accessories to current equipment, for example, safety buckets or containment rotors in centrifuges,
- dedicating current equipment for use only for the higher-risk tasks to avoid cross contamination, and
- using additional, dedicated safety equipment to protect against infectious aerosols – Biosafety Cabinets

3.8 Emergency/incident response

Even when carrying out low-risk work and following all core requirements for biosafety, incidents can still occur. To reduce the likelihood of exposure to/release of a biological agent or to reduce the consequences of such incidents, a contingency plan must be developed that provides specific SOPs to be followed in possible emergency scenarios that apply to the work and local environment. Personnel must be trained on these procedures and have periodic refresher training in order to maintain competency.

Emergencies can include those related to chemical incidents, fire, electrical breakdown, radiation incidents, pest infestation, flooding, or personal health issues of personnel (for example, a heart attack or collapse). All laboratory facilities must have good safety standards for all such non-biological hazards to make sure that necessary non- biological risk control measures are also in place (for example, fire alarms, extinguishers, chemical showers). Relevant authorities should be consulted where necessary.

First-aid kits, including medical supplies such as bottled eye washes and bandages, must be available and easily accessible to personnel. These must be checked routinely to make sure products are within their use-by dates and are in sufficient supply. If eyewash stations with piped water are to be used, these should also be checked regularly for correct functioning.

All incidents must be reported to the appropriate personnel, usually a laboratory supervisor, in a timely manner. A written record of accidents and incidents must be maintained, in line with national regulations where applicable. Any incident that occurs must be reported and investigated in a timely manner. Results from incident investigations must be used to update laboratory procedures and emergency response. More information on incident reporting and investigation can be found in section 7 biosafety program management and *Monograph: biosafety program management (17)*.

3.6.4 Biological spill response

Spill kits, including disinfectant, must be easily accessible to personnel. Depending on the size, location,

concentration and/or volume of the spill, different protocols may be necessary. Written procedures for cleaning and decontaminating spills must be developed for the laboratory and followed by suitably trained personnel.

If a spill occurs where there is a high initial risk (due to a large formation of aerosols, a large volume/high concentration of liquid spilt, and/or high pathogenicity of the biological agent involved) the following protocol should be followed:

- Personnel must immediately vacate the affected area.
- Exposed persons should be referred immediately for medical evaluation.
- The room containing the spill should not be entered for a length of time that allows aerosols to be carried away and heavier particles to settle. If the laboratory does not have a central air exhaust system, entrance should be delayed for longer.
- Signs must be posted indicating entry is forbidden.
- The laboratory supervisor and the biosafety officer must be informed as soon as possible after the event has occurred.
- After the necessary amount of time has elapsed, decontamination must proceed; depending on the size of the spill, this may require help or supervision, for example, by the biosafety officer.
- Suitable protective clothing and respiratory protection may be needed for the spill clean-up.

Heightened controls (spills)

- Planning for and sourcing of post-exposure prophylaxis and therapeutics that may be necessary.
- An emergency shower for staff.

Occupational health

The employing authority, through the laboratory director, must take responsibility for ensuring that the health of laboratory personnel is adequately checked and reported. The objective is to provide a safe working environment including preventative measures (for example, vaccination) and monitoring of employee health to enable appropriate measures to be taken in case of exposure or occupationally related disease or any other aspect of the work that affects the safety, health and well-being of employees.

Medical examination or health status information of laboratory personnel may be required to ensure

that it is safe for them to work in the laboratory. All aspects of an employee's health status must be kept confidential. Examples of activities to achieve these objectives can be found in *Monograph: biosafety program management (17)*.

Heightened controls (occupational health)

- Medical examination of all laboratory personnel who work with heightened control measures to determine their health status is not at risk in performing the work. This should include a detailed medical history and an occupationally-targeted examination, which should be recorded.
- Provision by the physician of a medical contact card with a medically cleared emergency point of contact in case a sudden illness occurs outside of work hours.
- Primary containment devices (table 4.1)

Table 4.1 (Heightened Control) Types and features of primary containment devices (biosafety cabinets)

Refer also to CPHL/FFCG Biosafety SOP G_90_SOP_8_A.

TYPE OF PRIMARY CONTAINMENT DEVICE	KEY FEATURES
Class I BSCs	▪ Open-fronted cabinets with an inward airflow designed to protect the operator and the environment from infectious aerosols generated. ▪ Simple airflow design allows performance maintenance in most laboratory situations. If specified with higher inflow rates, they may perform better than other BSC types in certain circumstances. ▪ The air discharged can be passed through an appropriate filter (for example, a HEPA filter) before being discharged or recirculated into the laboratory.
Class II BSCs	▪ Several different Class II BSCs exist, each of which has slightly different airflow arrangements and/or mechanisms. A brief overview of these can be found in Monograph: biological safety cabinets and other primary containment devices. ▪ One of the most commonly used BSCs in laboratory facilities is the Class II type A2 or an equivalent European standard type (CEN 12469). These open-fronted cabinets have a complex airflow pattern, which mixes inflow air with internally filtered downflow air. This provides protection to work surface materials, for example, cell cultures, in addition to users and the environment. ▪ The complex airflow of Class II BSCs means their performance can easily be affected by factors such as cabinet positioning, room ventilation rates and pressure differences. For this reason, Class I BSCs may be a more sustainable choice because of their simpler design and the robustness of their protection to the operator when product protection is not a major consideration. ▪ Air from the workspace is passed through an appropriate filter before discharge. This air can be recirculated to the room, discharged to the outside of the building through a thimble duct/canopy hood connection to a dedicated duct, or discharged through the building's heating, ventilation, and air conditioning exhaust system.

• BSC = biological safety cabinet; HEPA = high efficiency particulate air.

Section 4. Heightened Control Measures –integrated to Section 3

Relevant parts of Section 4 (heightened control measures) were integrated into Section 3 as above.

Section 5: Maximum Containment Measures - removed

Section 5 was removed from this version.

For the original section 5, refer to Laboratory biosafety manual, 4th edition (who.int) 2020.

Section 6. Transfer and Transportation

It is often necessary to transport specimens, biological materials or waste that are known or expected to contain biological agents between rooms, laboratories or facilities. In some cases, the material may need to be transported to laboratories in other cities, regions or even countries for further testing, treatment or storage. For the purpose of transport, materials from the laboratory that may contain biological agents are known as infectious substances; these include cultures, patient or animal specimens, infected body parts or organs, and biological products such as live attenuated vaccines or similar therapeutic products. Genetically modified organisms, if they are capable of causing infection in humans or animals, will also fall under this category.

Transportation of infectious substances may be subject to various national and/or international regulations, depending on the origin, destination and/or the mode of transport being used. Independent operators involved in the process (such as couriers, airlines or logistics services) may also request additional protocols. Irrespective of the regulations that apply, the aim is always to reduce the likelihood of an exposure to and/or a release of the infectious substance in order to protect personnel, the community and/or the surrounding environment.

Transferring or transporting infectious substances within or between laboratories should always be undertaken in a way that minimizes the potential for drop, spillage, collision or similar events. The following subsections provide an overview of the main issues to consider in the transfer or transport of infectious substance.

6.1 Transfer within the laboratory

Moving infectious substances within the laboratory, for example, from a BSC to an incubator, should be undertaken following GMPP to prevent incidents of cross contamination and inadvertent spillage. Additional measures to consider include the following:

- Use sealed containers, such as screw-capped tubes. Snap-cap lids should be avoided as they are less secure.
- Use deep-sided and leak-proof trays or boxes made of smooth impervious material (for example, plastic or metal), which can be effectively cleaned and disinfected.
- Locking plastic containers and storage containers are an option.
- If using racks, vials or tubes, trolleys can be used for more stable transport, as they are less likely to result in multiple spillages if a worker trips or falls.
- If using trolleys, ensure they are loaded so that substances cannot fall off, for example, by securing the load or using some form of guard rail or raised sides.
- Make sure spill kits are readily available for use in the event of a spillage during transfer, and available personnel are trained in their use.

6.2 Transfer within a building

In addition to the considerations above, the transfer of infectious substances between rooms, departments or laboratories in the same building must be planned, organized and carried out in a way that minimizes transit through communal areas and public thoroughfares.

Transfer containers must be suitably labelled to identify their contents, and surfaces decontaminated before leaving the laboratory. Biohazard symbols *(31)* should be used on containers as a heightened control measure, if the biological agent being handled is associated with a higher likelihood of infection.

6.3 Transfer between buildings on the same site

Issues that need to be considered for containers and layers of outer packaging to minimize the risks of leakage while transferring infectious substances between buildings are outlined below.

- Sealable plastic bags, plastic screw-top tubes and locking plastic containers can all be used in the transfer of infectious substances between buildings.
- In Figure 6.1 are examples of items that can be used for containment during transport. Redundant layers of packaging, as described in subsection 6.4.3, should be considered.
- Absorbent materials should be used between layers of packaging to absorb all infectious substances, if there were leakage.
- The outermost transport container should be rigid. It can vary widely depending on the resources available. A plastic box or small plastic ice chest (Figure 6.1.) is one option for the transport of infectious substances between buildings on the same site, as they are secure and easily decontaminated.

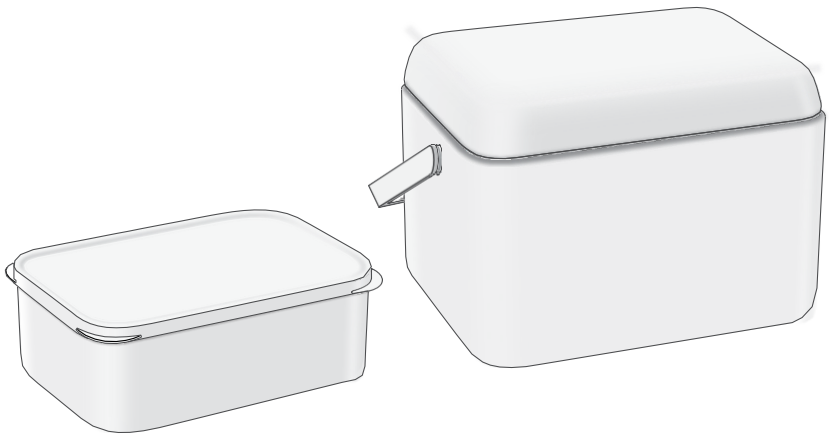

Figure 6.1 Containers for transfer of substances between buildings on the same site

- Packaging should be labelled in a way that the sender, recipient and contents of the package are clearly identifiable. It should include biohazard symbols where appropriate.
- Personnel involved in the transfer must be provided with suitable awareness training on the risks present during the transfer process and how to safely reduce them.
- Spill kits must be readily available and appropriate personnel trained in their use.
- Recipients must be notified in advance of the transfer occurring.

6.4 Off-site transport of infectious substances

In some cases, infectious substances must be transported off-site for further processing, storage or disposal. This includes transport between sites of the same organization and from one organization to another. People at risk during off-site transportation are not only those involved in the transport, but also the public whose path might be crossed in transit. For this reason, ensuring infectious substances are safely contained and handled may be of interest to local, national and/or international authorities.

Different national and international transport regulations have been developed to regulate packaging, labelling, marking and documentation of infectious substances to minimize the likelihood of exposure and/or release during transit. Most national regulations are adapted from the *United Nations Model Recommendations on the Transport of Dangerous Goods (32)* and overseen by

independent compliance organizations or national authorities.

For transport purposes, these regulations classify materials that (may) contain biological agents as dangerous goods, under the class of “toxic and infectious substances”. Infectious substances are then further classified, based on a pathogen risk assessment, into subgroups for which different procedures are stipulated.

Other regulations may also apply to the shipment depending on the mode of transportation being used, if other dangerous goods are also present, and whether any national regulations are stipulated by the country of origin and/or the country receiving the shipment, including import or export licences as applicable.

The following subsections provide a short introduction to the regulations, classifications and safety controls that may be applied to the off-site transport of infectious substances. For more detailed information, please refer to documents listed in the reference section.

6.4.1 Regulation of the transport of infectious substances

Most of the regulations for the transport of infectious substances are based upon the United Nations (UN) model regulations *(32)*. These regulations, reviewed every two years, should be consulted regularly to ensure that a laboratory’s protocols for packaging, labelling, marking and transporting infectious substances comply with the current regulations. However, as these regulations are not intended to supersede any local or national requirements, and it is possible some national variations exist, national regulations for transport should always be consulted first.

Other international regulations for the transport of infectious substances include modal transport agreements, with variations for air *(33,34)*, sea *(35)* and land *(36,37)* transportation. If national requirements do not exist, these modal agreements should be followed. Where multiple regulations exist, the more stringent ones must be applied. Other regulations or requirements may also apply to infectious substances if they are transported with other dangerous goods, including cooling materials such as dry ice or liquid nitrogen. Import and export requirements should also be considered, as should the application of other international agreements, for example, material transfer agreements where applicable *(38)*.

Ultimately, it is the responsibility of the personnel sending the infectious substance (often referred to as the “shipper”) to ensure that they are familiar with all applicable regulations and/or variations that apply to their shipment and that they comply with them. Shippers must consult the relevant authorities to determine whether they are able to comply with these requirements before starting the shipment process.

All personnel who participate in any part of the transport of a dangerous good, including infectious substances, must have training on the applicable regulations to a proficiency level appropriate for their job responsibilities.

This may include general familiarization and awareness training, functional training on packaging, labelling and documentation, and safety training including best practice for handling dangerous goods to avoid incidents as well as emergency/incident response information. For certain types of infectious substances, a formal certification may be legally required, proving competence in these areas.

6.3.1 Classification of infectious substances

For transport purposes, infectious substances (cultures, human or animal specimens, biological products such as live-attenuated vaccines, infectious genetically modified organisms or medical/clinical wastes) may be further subdivided into the following classifications based on the pathogenicity of the biological agent it contains (or is suspected to contain): Category A, Category B and Exempt human/animal specimens. Each classification is assigned identifiers which includes a proper shipping name, and/or a

unique four-digit UN number *(32)*, which can be used to clearly identify the substance composition and hazardous nature of the biological agent, and indicate the specific transport requirements to be applied.

A brief introduction to infectious substances classifications and summary of the physical and procedural risk control measures that may apply are given below.

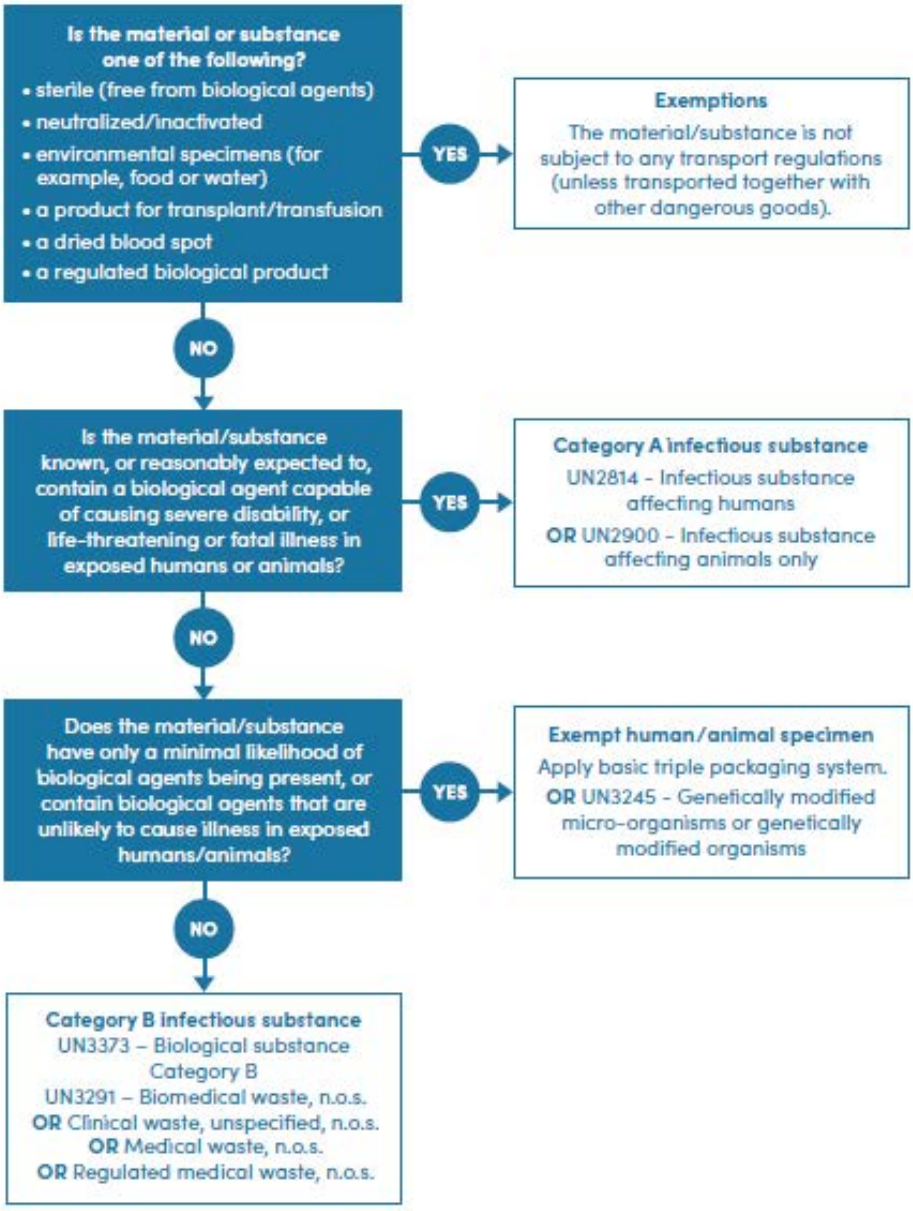

Figure 6.2 Classification of infectious substances for transportation

Figure 6.2 above also shows a flowchart which summarizes the various classifications and their features. More specific information on transport requirements can be found in the WHO guidance on the shipment of infectious substances (39) or should be sought from applicable regulations and agreements, depending on the transport conditions.

Category A and B infectious substances

Categories A and B infectious substances are the two most important classifications used when transporting biological agents (or material containing biological agents) off the laboratory site. The main

difference between the two classifications relates to the consequences (severity of outcomes) of an infection with the biological agent being transported if an incident were to occur while in transit.

Category A infectious substances are defined as any material(s) known or reasonably expected to contain, biological agents capable of causing permanent disability, or life- threatening or fatal disease in otherwise healthy humans or animals. For the purposes of transport, these substances carry the highest biosafety and biosecurity risks and are therefore subject to the largest number of risk control measures, including regulated packaging of materials in a triple layer configuration, strict labelling criteria and detailed documentation processes. All people involved in the shipment of Category A infectious substances must be formally certified by an appropriate authority as determined by the relevant regulations.

An indicative list of the biological agents included in Category A can be found in the relevant regulations on transport of infectious substances *(32-37)*, and in the WHO guidance document on this subject *(39)*.

However, the indicative list of biological agents is not exhaustive and does not include new or emerging pathogens whose properties are unknown. In this case, classification must be based on available clinical evidence, local endemic conditions, the source of the infectious substance and sound medical judgement. If there is any doubt as to whether a substance meets the criteria, it must be considered Category A for transport purposes.

Category B infectious substances are defined as any material(s) containing biological agents capable of causing infection in humans or animals, but which do not meet the criteria for inclusion in Category A. These substances are also subject to strict regulation, including a triple-layer of packaging materials, special labelling and documentation. However, these are generally less stringent than for Category A infectious substances, depending on the applicable national regulations.

A summary of the main requirements for the classification, identification, packaging, labelling and documentation when transporting Category A and Category B infectious substances is provided in Table 6.1.

Table 6.1 Summary categorization, documentation, packaging and labelling of infectious substances for transport

	CATEGORY A	CATEGORY B
Definition	Containing a biological agent known, or reasonably expected, to cause permanent disability, or life-threatening or fatal disease	Containing a biological agent capable of causing infection in susceptible humans or animals, but which does not meet the criteria for inclusion in Category A
Identifiers (UN number and proper shipping name)	▪ UN2814: Category A infectious substances (affecting humans or zoonotic infectious substances) ▪ UN2900: Category A Infectious substances (affecting only animals) ▪ UN3549: Category A solid medical waste	▪ UN3291: Category B clinical ormedical waste ▪ UN3373: Category B infectious substances (for all other substances or materials including human or animal material, cultures and biological products)
Documentation	▪ An itemized list of contents (placed between the secondary and outer packaging) ▪ Names and addresses of the shipper and the receiver ▪ A dangerous goods transport document (dangerous goods declaration) ▪ Additional documentation may be required depending on the modal requirements (for example, air waybill for air shipments) or national regulations (for example, import/ export permits)	▪ An itemized list of contents (placed between the secondary and outer packaging) ▪ Names and addresses of the shipper and the receiver ▪ Additional documentation may be required depending on the modal requirements (for example, air waybill for air shipments) and/or other national requirements (for example, import/export permits)
Packaging	▪ Triple packaging required to comply with UN packing instruction P620 ▪ Packaging must show a UN specification mark, indicating compliance with testing requirements for Category A infectious substances packaging	▪ UN3291: single packaging acceptable provided that: enough absorbent material is present to absorb the entire amount of liquid, the package is leak-proof, and/ or any sharp items are contained within puncture-resistant packaging ▪ UN3373: Triple packaging required (for air transport, either the secondary or outer package must be rigid) which complies with and is packaged according to UN packing instruction P650

UN = United Nations.

Exempt human (or animal) specimens

Substances or materials derived from human or animal patients (that are clinical specimens) for which there is a minimal likelihood that infectious biological agents are present, are defined as exempt human or exempt animal specimens. This means they are exempt from many of the stringent criteria applied to Category A and Category B infectious substances, especially for marking, labelling and documentation. However, exempt specimens are still required to be packaged using redundant layers of packaging in a triple-layered system containing primary, secondary and outer packaging of adequate strength for the substance being transported.

Triple packaging for exempt specimens must be capable of preventing leakage of any and all liquid material held inside, and should be clearly marked on the outside with either Exempt Human Specimen or Exempt Animal Specimen as appropriate. If exempt specimens are being transported with other substances that meet the criteria for inclusion in another dangerous goods class, such as dry ice or other infectious substances, the relevant regulations for those substances must be followed.

Exclusions

Some biological materials being transported off the laboratory site are known to be free of, or are extremely unlikely to contain, any biological agents.

Such materials are excluded from any regulation on packaging, marking, labelling or documentation. These exclusions include:

- materials known to be free of infectious substances,
- biological agents within the material that have been inactivated or destroyed,
- biological agents within the material that are not pathogenic to humans or animals,
- dried blood spot or faecal occult blood specimens transported for analysis,
- environmental specimens not considered to be a significant hazard to health, and
- items for transplant or transfusion.

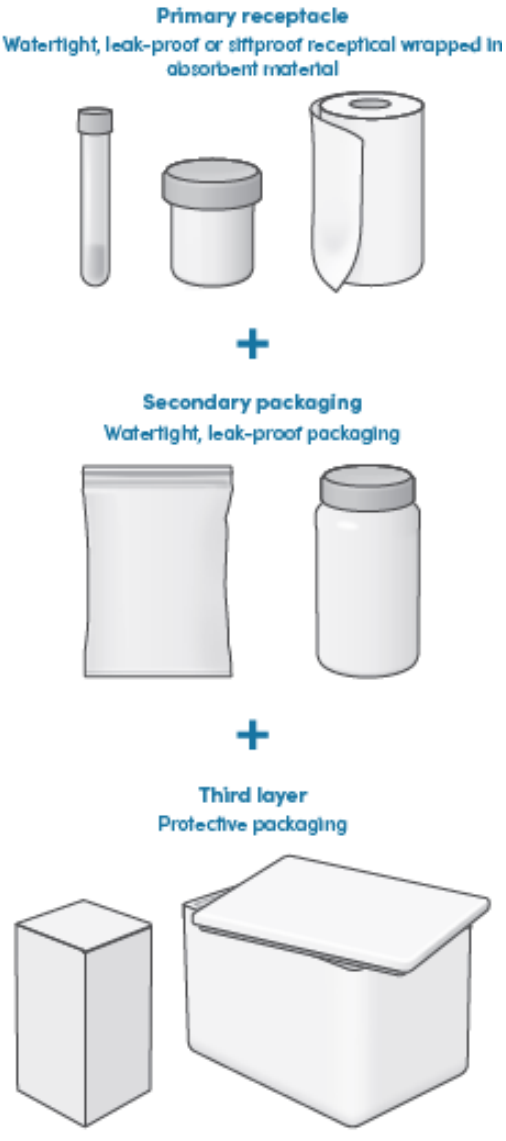

Figure 6.3 Example of triple packaging for infectious substances

6.4.3 Triple packaging of infectious substances

Using redundant layers of packaging is a common method for controlling any leakage or breach of containment of an infectious substance to reduce the likelihood of exposure and/or release during transport. A triple packaging system is commonly recommended, and required by regulation, for all three classifications of infectious substances described in the previous sections.

A triple package consists of three layers (see example in Figure 6.3). The primary receptacle, containing the infectious substance must be watertight, leak-proof and appropriately labelled as to its contents. The primary receptacle must be wrapped in enough absorbent material to absorb its contents in the event spillage occurs. If multiple primary receptacles are packed together, cushioning material must be used to prevent contact between them.

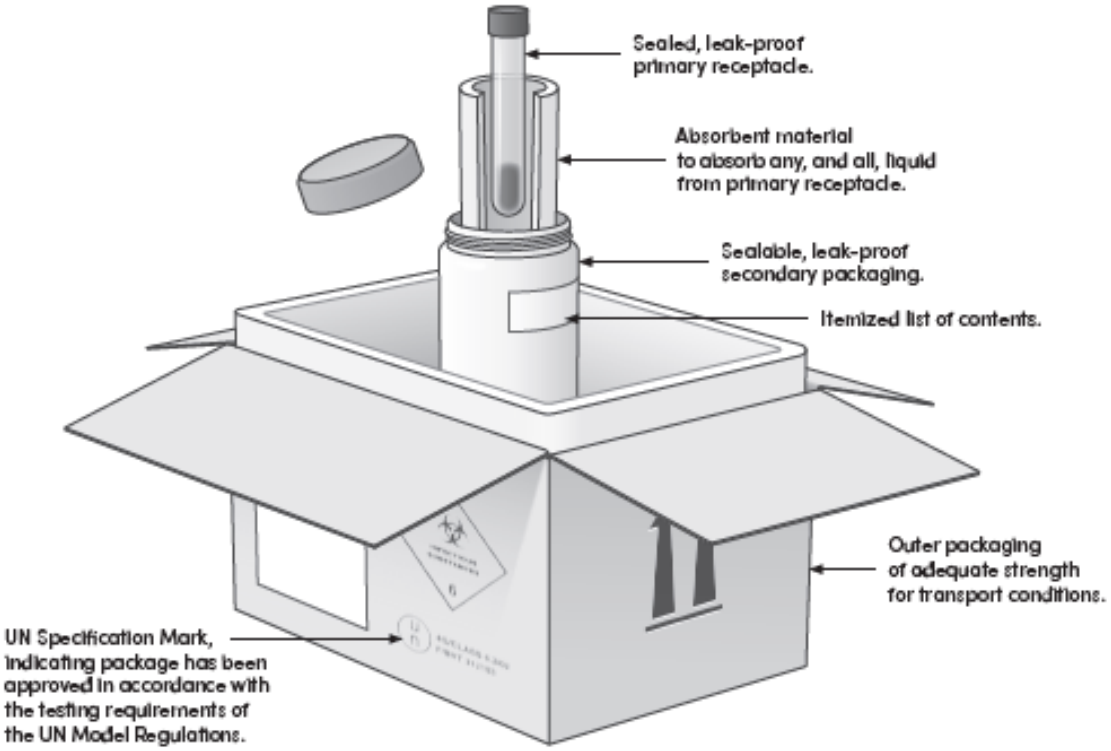

Figure 6.4 Exampple of triple packaging materials suitable for Category A infectious substances

Secondary watertight, leak-proof packaging is used to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in a single secondary packaging. Some regulations may have volume and/or weight limits for packaged infectious substances.

The third layer protects the secondary packaging from physical damage while in transit. It is between the second and third outer layers that coolants, such as dry ice or liquid nitrogen, can be used if necessary. Such coolants are also classified as dangerous goods and may therefore be subject to additional requirements themselves, as outlined in applicable regulations. For example, when dry ice is used, the third layer must be capable of releasing carbon dioxide gas to prevent explosion. Specimen data forms, letters and other types of information that identify or describe the infectious substance and identify the shipper and receiver, and any other documentation required, must also be provided according to current applicable regulations.

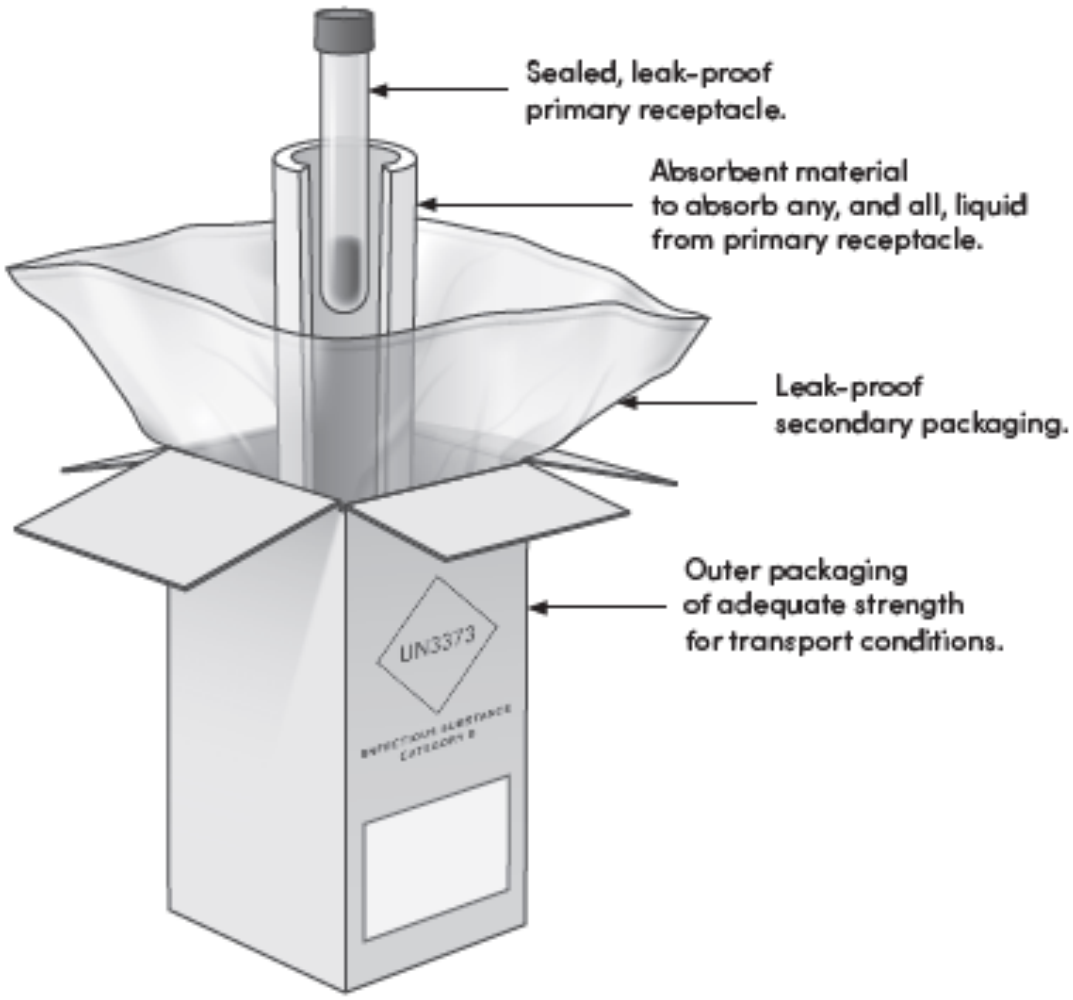

Figure 6.5 Example of triple packaging materials suitable for Category B infectious substances

The outer layer of the triple package must also be marked and labelled appropriately, to provide the correct information about the hazards of the packaged contents for both for the infectious substance and any other dangerous goods that may be present, such as dry ice. General shipping information, such as the shipper and receiver of the infectious substance, and handling information, such as orientation arrows on the box, may also be required. As the exact requirements for the composition of the triple packaging may differ depending on the classification of the substance and mode of transport being used, applicable regulations must always be consulted to ensure the correct materials are used.

More detailed information on the specific transport requirements for categories A and B infectious substances is provided in the UN model regulations *(32)* as guidance's known as "packing instructions" . These prescribe the components of packaging that must be used for various dangerous goods classes, as well as the standards that the material must meet to be approved for use. There are two different packing instructions that relate to infectious substances. P620 applies to all Category A shipments (both UN2814 and UN2900). It provides additional requirements to the basic triple packaging system. These include criteria to comply with rigorous package testing that demonstrate the ability to withstand internal pressures without leakage, and to withstand dropping, stacking and even conditioning (such as with water and temperature extremes). P620 also describes additional packaging requirements for shipments that include dry ice. An example of packaging material for Category A infectious substances is shown in Figure 6.4.

A more basic triple packaging system P650 applies for the transport of other classifications of infectious substances–Category B (Figure 6.5) or exempt human and animal specimens. Packaging compliant with P650 must also undergo drop-testing and internal pressure testing in some situations, although this is less stringent than that required for Category A infectious substance packaging.

Section 7. Biosafety Program Management

The effective management of biological risks is supported by established measures at both the national and institutional levels. Just as national governments and authorities must assess biological risks and apply nation-wide regulatory frameworks to control them, organizations in which biological agents are handled have an obligation to assess the biological risks that exist in their facility and apply appropriate risk control measures to protect their personnel, community and the environment.

A structured oversight system for managing biological risks implemented at the national level (for example, a regulatory framework) will inform and direct the mechanisms by which organizations can meet their related obligations. Organization- specific risk assessments can further guide the selection and implementation of appropriate risk control measures and mitigation strategies that reduce risks to acceptable . The management of this process requires an organization to develop a biosafety program: a set of tools, information and associated actions that are overseen, and continuously improved upon, by an organization's senior management.

Effective management of a structured biosafety program ensures the following activities have been undertaken.

- There is a commitment from senior management to appropriately address and manage the risks associated with the biological agents being handled.
- All risks associated with work activities have been identified, understood and controlled to an acceptable and practical level.
- Practice and procedure necessary to control risks have been put in place and are monitored regularly to ensure continued effectiveness and relevance.
- A framework has been developed for the appropriate training of personnel in biosafety practices and biosecurity awareness.
- The roles and responsibilities of all personnel are clearly set out and understood.
- Activities related to laboratory biosafety, and its associated policies and procedures, are aligned with national and international guidelines and regulations.

A biosafety program is often a component of an overarching safety program at the organizational level (that is one that holistically assesses and addresses all types of health and safety risk within an organization).

However, the independence of the biosafety program and its management from the organizational governance structure will depend on the size and complexity of the facility. For example, a standalone biosafety program may be necessary where high risks exist, or where complex or broad types of activities with biological material are conducted.

This section provides an overview of the foundational elements of a biosafety program and how these can be managed at an institutional level. While the size and complexity of an organization dictates the specifics of a biosafety program, these foundational elements, when based on a strong biosafety culture, provide a solid framework for the most effective biosafety program.

Additional information and guidance on how to successfully implement and manage a biosafety program can be found in Monograph: biosafety program management (17).

7.1 Biosafety culture

Biosafety culture is the set of values, beliefs and patterns of behaviour instilled and facilitated in an open and trusting environment by individuals throughout the organization who work together to support or enhance best practice for laboratory biosafety. This culture is crucial for the success of a biosafety

program, and is built from mutual trust and the active engagement of all personnel across the organization, with a clear commitment from the organization's management. Establishing and maintaining a biosafety culture provides a foundation upon which a successful biosafety program can be developed.

7.2 Biosafety policy

An institutional biosafety policy is a document that describes the scope, purpose and objectives of the biosafety program. A biosafety policy in place is a demonstration of the prominence of and commitment to biosafety within the organization.

7.3 Assigned roles and responsibilities

Although the responsibility for establishing and managing a biosafety program, including defining and assigning roles and responsibilities, rests with the senior management of an organization, all facility personnel who may come into contact with biological agents are responsible for actively participating in the biosafety program. Succession planning should be in place for management, scientific, technical and administrative personnel to ensure that critical knowledge of the safe and secure operation of the facility does not lie with just one individual in the event of unavailability or departure.

The various roles and responsibilities that should be assigned to personnel in order to successfully manage a biosafety program are outlined in the following subsections.

7.3.1 Senior management

Senior management is responsible for the creation of policies and guidelines, as well as for the ongoing support of the biosafety program. They are responsible for ensuring funding to support the program and for providing oversight of the implementation and ongoing review of the program components.

7.3.2 Biosafety committee

A biosafety committee is an institutional committee created to act as an independent review group for biosafety issues; it reports to senior management. The membership of the biosafety committee should reflect the different occupational areas of the organization as well as its scientific expertise.

7.3.3 Biosafety officer

A biosafety officer should be appointed to provide advice and guidance to personnel and management on biological safety issues. The role and knowledge of the biosafety officer is key to developing, implementing, maintaining and continually improving a biosafety and biosecurity program. Biosafety officers should have sufficient training and experience so that they are competent to perform the role, and they should be allocated enough time and resources to do the job effectively. However, depending on the size and nature of the laboratory, the biosafety officer could be a contractor or could perform the duties part time.

7.3.4 Laboratory personnel and support personnel

All personnel within the organization who have access to the laboratory space or to the biological agents in the facility are responsible for supporting and contributing to a biosafety program. The laboratory director/manager is responsible for implementing and promoting biosafety to ensure the safety of all personnel, contractors and visitors to the facility, and to protect the public and the

environment from hazards arising from the work being performed in the laboratory. Laboratory and support personnel are responsible for applying biosafety in their daily activities.

7.4 Biosafety manual

A biosafety manual is a mandatory collection of all the organization-specific documents that describe the foundational elements of their biosafety program. These may include policies, information about supporting programs and plans, and organization-specific SOPs.

7.5 Biosafety and biosecurity risk assessment

The main goal of a biosafety program is to effectively manage biological and biosecurity risks. An essential activity to achieve this objective is conducting risk assessments. A biosafety/biosecurity risk assessment is a systematic process of gathering and 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, please refer to section 2 risk assessment. Templates and additional guidance can also be found in Monograph: risk assessment (18), and Monograph: biosafety program management (17).

7.6 Supporting programs and plans

The outcomes of biosafety and biosecurity risk assessments will inform the selection of risk control measures that are needed to address identified risks. The correct implementation of these measures must then be managed through the development and management of several supporting programs or systems. The details of these need to be accessible to personnel through the biosafety manual, and which may include:

- biosecurity plan and laboratory access system,
- occupational health program,
- personnel management and training program,
- SOP development,
- facility design plans,
- laboratory equipment purchase, installation and maintenance plan,
- decontamination and waste management system,
- emergency/incident response,
- record and document management system,
- inventory control plan, and
- communication plan.

The development and approval of these supporting programs and plans are directed by senior management, with the support of relevant expertise (for example, biosafety officer, biosafety committee, engineers, facility-specific management).

Descriptions and key considerations for the biosafety manual and each of the supporting programs and plans can be found in *Monograph: biosafety program management (17)*. Key risk control strategies that need to be included in these plans can be found in section 3 core requirements, section 4 heightened control measures and section 5 maximum containment measures.

7.7 Reports and reviews

Biosafety programs are dynamic and require regular assessment and flexible strategies to ensure ongoing and sustained improvement. The biosafety program must be reviewed periodically to ensure continued suitability, adequacy and effectiveness. To do this, it is essential that organizations have record-keeping and review systems which must include the features outlined in the following subsections.

7.7.1 Incident reporting and investigation

Assessments of the type and severity of incidents, including those that do not result in exposure or release (that are near misses), that may occur in the laboratory provide key information to guide the nature and scope of responses and future preparedness.

Performing a thorough review of all incident reports is an important part of biosafety program management because it provides information on what worked and what did not. It also provides an opportunity to perform a root cause analysis to identify any underlying factor(s) that might have increased the likelihood of the incident (or near miss) occurring. Results from incident investigations should be used to update and improve emergency response, and are a training opportunity on lessons learned to prevent future occurrences.

7.7.2 Audits and inspections (internal and external)

Many laboratories implement a cooperative inspection program where laboratory personnel are directly responsible for periodic self-audits (self-assessments) coupled with a less frequent, but more in-depth, evaluation with the biosafety officer and/or members of the biosafety committee. In some cases, laboratories may also have external audits and/or inspections, for example, as part of a certification process, under the national regulatory framework, or in an international mentoring program. These assessments can provide information on the effectiveness of a biosafety program, and the results can be analysed to identify weaknesses that may need to be addressed.

7.7.3 Other reports

In addition to incident reports and laboratory assessments, a biosafety program may also record and review other information such the outcomes of training exercises and drills and employee surveys in order to identify additional biosafety improvement opportunities.

Further guidance on and templates useful for the improvement and review of the biosafety program can be found in Monograph: biosafety program management (17).Section 8.

Section 8. Laboratory Biosecurity - abridged

Laboratory biosecurity refers to institutional and personnel security measures designed to prevent the loss, theft, misuse, diversion or intentional release of biological agents being handled in the laboratory. Addressing laboratory biosecurity risks in many ways parallels and complements that of biosafety risk management. Effective biosafety practices are the foundation of laboratory biosecurity and biosecurity risk control measures must be performed as an integral part of an institution's biosafety program management.

For the complete section 8, refer to Laboratory biosafety manual, 4th edition (who.int) 2020.

Section 9. National / International Biosafety Oversight -removed

Section 9, NATIONAL / INTERNATIONAL BIOSAFETY OVERSIGHT has been removed from this document. Refer to Laboratory biosafety manual, 4th edition (who.int) 2020.

Glossary

Acceptable risk: The risk that is considered acceptable and allows work to proceed bearing in mind the expected benefit of the planned activities.

Accident: An inadvertent occurrence that results in actual harm such as infection, illness, injury in humans or contamination of the environment.

Aerosol: Liquid or solid particles suspended in air and of a size that may allow inhalation into the lower respiratory tract (usually less than 10 micrometres in diameter).

Aerosol/airborne transmission: The spread of infection caused by the inhalation of aerosols.

Aerosol-generating procedure: Any procedure that intentionally or inadvertently results in the creation of liquid or solid particles, which become suspended in the air (aerosols).

Aseptic techniques: Conditions and procedural measures designed to effectively prevent contamination.

Biological agent: A microorganism, virus, biological toxin, particle or otherwise infectious material, either naturally occurring or genetically modified, which may have the potential to cause infection, allergy, toxicity or otherwise create a hazard to humans, animals, or plants.

Biological safety cabinet (BSC): An enclosed, ventilated working space designed to provide protection to the operator, the laboratory environment and/or the work materials for activities where there is an aerosol hazard. Containment is achieved by segregation of the work from the main area of the laboratory and/or through the use of controlled, directional airflow mechanisms. Exhaust air is passed through a high efficiency particulate air (HEPA) filter before recirculating into the laboratory or into the building's heating, ventilation and air conditioning system. There are different classes (I, II and III) of BSCs that provide different levels of containment.

Biosafety: Containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents or their inadvertent release.

Biosafety committee: An institutional committee created to act as an independent review group for biosafety issues, reporting to senior management. The membership of the biosafety committee should reflect the different occupational areas of the organization as well as its scientific expertise.

Biosafety officer: An individual designated to oversee facility or organizational biosafety (and possibly biosecurity) programs. The person fulfilling this function may also be termed biosafety professional, biosafety advisor, biosafety manager, biosafety coordinator, or biosafety management advisor.

Biosafety program management: The development, implementation and oversight of biosafety at the organizational level using a variety of information that includes institutional policies, guidance documents for practices and procedures, planning documents (training, recruitment, emergency/incident response) and record keeping (personnel, inventories, incident management).

Biosecurity: Principles, technologies and practices that are implemented for the protection, control and accountability of biological materials and/or the equipment, skills and data related to their handling. Biosecurity aims to prevent their unauthorized access, loss, theft, misuse, diversion or release.

Calibration: Establishment of the relationship between the measurement provided by the instrument and the corresponding values of a known standard, allowing correction to improve accuracy. For example, laboratory equipment such as pipetting devices may need calibration

periodically to ensure proper performance.

Certification: A third-party testimony based on a structured assessment and formal documentation confirming that a system, person or piece of equipment conforms to specified requirements, for example, to a certain standard.

Code of practice (code of conduct, code of ethics): Non-legislated guidelines for behavioural and practical standards that are voluntarily accepted as best practice and are thus followed by one or more organizations and/or individuals.

Communicability: Capability of a biological agent to be transmitted from one person or animal to another, either through direct or indirect transmission. This is often related to/represented by an epidemiological measurement called the basic reproduction number (R_0) which is an average number of secondary infections generated by a single infected individual in a fully susceptible population.

Consequence (of a laboratory incident): The outcome of an incident (exposure to and/ or release of a biological agent) of varying severity of harm, occurring in the course of laboratory operations. Consequences may include a laboratory-associated infection, other illness or physical injury, environmental contamination, or asymptomatic carriage of a biological agent.

Containment: The combination of physical design parameters and operational practices that protect personnel, the immediate work environment and the community from exposure to biological agents. The term "biocontainment" is also used in this context.

Core requirements: A set of minimum requirements defined in the fourth edition of the World Health Organization (WHO) *Laboratory biosafety* manual to describe a combination of risk control measures that are both the foundation for, and an integral part of, laboratory biosafety. These measures reflect international standards and best practice in biosafety that are necessary to work safely with biological agents, even where the associated risks are minimal.

Decontamination: Reduction of viable biological agents or other hazardous materials on a surface or object(s) to a pre-defined level by chemical and/or physical means.

Disinfectants: Agents capable of eliminating viable biological agents on surfaces or in liquid waste. These will have varying effectiveness depending on the properties of the chemical, its concentration, shelf life and contact time with the agent.

Disinfection: A process to eliminate viable biological agents from items or surfaces for further safe handling or use.

Droplets: A suspension of particles, normally defined as more than 10 micrometres in diameter, which tends to fall out of the air resulting in contamination of nearby surfaces.

Dual use items: Certain materials, information and technologies that are intended for benefit, but which might be misapplied to do harm.

Emergency/incident response: An outline of the behaviours, processes and procedures to be followed when handling sudden or unexpected situations, including exposure to or release of biological agents. The goal of an emergency/incident response is to prevent injuries or infections, reduce damage to equipment or the environment, and accelerate resumption of normal operations.

Endemic disease: A disease naturally occurring in a particular region or population.

Engineering controls: Risk control measures that are built into the design of a laboratory or laboratory equipment to contain the hazards. Biological safety cabinets (BSCs) and isolators are forms of engineering

control in order to minimize the risk of exposure to and/or unintended release of biological agents.

Exotic disease: A disease not normally occurring in a particular region or area, often imported from another area. It can also be referred to as non-indigenous disease.

Exposure: An event during which an individual comes in contact with, or is in close proximity to, biological agents with the potential for infection or harm to occur. Routes of exposure can include inhalation, ingestion, percutaneous injury and absorption and are usually dependent upon the characteristics of the biological agent. However, some infection routes are specific to the laboratory environment and are not commonly seen in the general community.

Good microbiological practice and procedure (GMPP): A basic laboratory code of practice applicable to all types of laboratory activities with biological agents, including general behaviours and aseptic techniques that should always be observed in the laboratory. This code serves to protect laboratory personnel and the community from infection, prevent contamination of the environment, and provide protection for the work materials in use.

Hazard: An object or situation that has the potential to cause adverse effects when an organism, system or (sub)population is exposed to it. In the case of laboratory, biosafety, the hazard, is defined as biological agents which have the potential to cause adverse effects to personnel and/or humans, animals, and the wider community and environment. A hazard does not become a "risk" until the likelihood and consequences of that hazard causing harm are taken into account.

Heightened control measures: A set of risk control measures as described in the WHO *Laboratory biosafety manual* that may need to be applied in a laboratory facility because the outcome of a risk assessment indicates that the biological agents being handled and/or the activities to be performed with them are associated with a risk that cannot be brought below an acceptable risk with the core requirements only.

Inactivation: Removal of the activity of biological agents by destroying or inhibiting reproductive or enzyme activity.

Incident: An occurrence that has the potential to, or results in, the exposure of laboratory personnel to biological agents and/or their release into the environment that may or may not lead to actual harm.

Infectious dose: The amount of biological agent required to cause an infection in the host, measured in number of organisms. Often defined as the ID_{50}, the dose that will cause infection in 50% of those exposed.

Infectious substances: The term applied for the purposes of transport to any material, solid or liquid, which contains biological agents capable of causing infection in either humans, animals or both. Infectious substances can include patient specimens, biological cultures, medical or clinical wastes and/or biological products such as vaccines.

Initial risk: Risk associated with laboratory activities or procedures that are conducted in the absence of risk control measures.

Laboratory-associated infection: Any infection acquired or reasonably assumed as a result of exposure to a biological agent in the course of laboratory-related activities. A person-to-person transmission following the incident may result in linked secondary cases. Laboratory-associated infections are also known as laboratory-acquired infections.

Likelihood (of a laboratory incident): The probability of an incident (that is exposure to and/or a release of a biological agent) occurring in the course of laboratory work.

Maximum containment measures: A set of highly detailed and stringent risk control measures

described in the fourth edition of the WHO *Laboratory biosafety manual* that are considered necessary during laboratory work where a risk assessment indicates that the activities to be performed pose very high risks to laboratory personnel, the wider community and/or the environment, and therefore an extremely high level of protection must be provided. These are especially needed for certain types of work with biological agents that may have catastrophic consequences if an exposure or release were to occur.

One Health: An approach to designing and implementing programs, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes. The areas of work in which a One Health approach is particularly relevant include food safety, the control of zoonoses, and combatting antibiotic resistance.

Pathogen: A biological agent capable of causing disease in humans, animals or plants.

Personal protective equipment (PPE): Equipment and/or clothing worn by personnel to provide a barrier against biological agents, thereby minimizing the likelihood of exposure. PPE includes, but is not limited to, laboratory coats, gowns, full-body suits, gloves, protective footwear, safety glasses, safety goggles, masks and respirators.

Primary containment device (equipment): A contained workspace designed to provide protection to its operator, the laboratory environment and/or the work materials for activities where there is an aerosol hazard. Protection is achieved by segregation of the work from the main area of the laboratory and/or through the use of controlled, directional airflow mechanisms. Primary containment devices include biological safety cabinets (BSCs), isolators, local exhaust ventilators and ventilated working spaces.

Propagation: The action of intentionally increasing or multiplying the number of biological agents.

Prophylaxis: Treatment given to prevent infection or to mitigate the severity of the disease if infection were to occur. It can be delivered before possible exposure or after exposure before the onset of infection.

Redundancy: Repetitions of systems or parts of a system to provide protection in the case of a primary system failure. For example, a series of high efficiency particulate air (HEPA) filters in case one or more fail when used to move laboratory air to the outside environment.

Residual risk: Risk that remains after carefully selected risk control measures have been applied. If residual risk is not acceptable, it may be necessary to apply additional risk control measures or to stop the laboratory activity.

Risk: A combination of the likelihood of an incident and the severity of the harm (consequences) if that incident were to occur.

Risk assessment: A systematic process of gathering information and evaluating the likelihood and consequences of exposure to or release of workplace hazard(s) and determining the appropriate risk control measures to reduce the risk to an acceptable risk.

Risk communication: An interactive and systematic process to exchange information and opinion on risk(s) that inclusively engages all relevant personnel of various categories as well as community leaders and officials where appropriate. Risk communication is an integral and ongoing part of the risk assessment, soliciting clear understanding of the risk assessment process and outcomes, aiming at proper implementation of risk control measures. Decisions on risk communication, including what, whom and how, should be part of an overall risk communication strategy.

Risk control measure: Use of a combination of tools, which include communication, assessment, training, and physical and operational controls, to reduce the risk of an incident/event to an acceptable risk. The risk assessment cycle will determine the strategy that should be used to control the risks and the specific types of risk control measures required to achieve this.

Risk evaluation: Part of risk assessment where the likelihood of exposure to a hazard is weighed against the potential severity of harm under a set of predefined circumstances, such as a specific laboratory procedure. The goal of a risk evaluation is to determine whether the assessed risk is acceptable, or whether further targeted risk control measures should be implemented to prevent or reduce the risks.

Safety culture: A set of values, beliefs and patterns of behaviour instilled and facilitated in an open and trusting atmosphere by individuals and organizations working together to support or enhance best practice for laboratory biosafety, irrespective of whether it is stipulated in applicable codes of practice and/or regulations.

Sharps: Any device or object that is a puncture or wound hazard because of its pointed ends or edges. In the laboratory, sharps can include needles, syringes with attached needles, blades, scalpels or broken glass.

Standard operating procedures (SOPs): A set of well-documented and validated stepwise instructions outlining how to perform laboratory practices and procedures in a safe, timely and reliable manner, in line with institutional policies, best practice and applicable national or international regulations.

Sterile: The state of having a complete absence of viable biological agents and spores.

Sterilization: A process that kills and/or removes all biological agents including spores.

Transmission: The transfer of biological agent(s) from objects to living things, or between living things, either directly or indirectly via aerosols, droplets, body fluids, vectors, food/water or other contaminated objects.

Validation: Systematic and documented confirmation that the specified requirements are adequate to ensure the intended outcome or results. For example, in order to prove a material is decontaminated, laboratory personnel must validate the robustness of the decontamination method by measurement of the remaining biological agents against the detection limit by chemical, physical or biological indicators.

Verification: Confirmation that a given item (product, process or system) satisfies the specified requirements. For example, verification that the performance of an autoclave meets the standards specified by the manufacturer should be performed periodically.

Zoonotic disease (zoonosis): Infectious disease that is naturally transmitted from animals to humans and vice versa.

References

1. World Health Organization. Laboratory biosafety manual. First edition. Geneva: World Health Organization; 1983

2. World Health Organization. Laboratory biosafety manual. Second edition. Geneva: World Health Organization; 1993

3. World Health Organization. Laboratory biosafety manual. Third edition. Geneva: World Health Organization; 2004

4. Wurtz N, Papa A, Hukic M, Di Caro A, Leparc-Goffart I, Leroy E, et al. Survey of laboratory-acquired infections around the world in biosafety level 3 and 4 laboratories. Eur J Clin Microbiol Infect Dis. 2016 Aug;35(8):1247-58. doi: 10.1007/ s10096-016-2657-1

5. Choucrallah D, Sarmiento L, Ettles S, Tanguay F, Heisz M, Falardeau E. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2018. Can Commun Dis Rep. 2019 Sep 5;45(9):244-51. doi: 10.14745/ccdr.v45i09a04

6. Sejvar JJ, Johnson D, Popovic T, Miller JM, Downes F, Somsel P, et al. Assessing the risk of laboratory-acquired meningococcal disease J Clin Microbiol. 2005 Sep;43(9):4811-4. doi: 10.1128/JCM.43.9.4811-4814.2005

7. Barry M, Russi M, Armstrong L, Geller D, Tesh R, Dembry L, et al. Brief report: treatment of a laboratory-acquired Sabiá virus infection. N Engl J Med. 1995 Aug3;333(5):294-6. doi: 10.1056/NEJM199508033330505

8. Bouza E, Sanchez-Carrillo C, Hernangomez S, Gonzalez MJ. Laboratory-acquired brucellosis: a Spanish national survey. J Hosp Infect. 2005 Sep;61(1):80-3. doi: 10.1016/j.jhin.2005.02.018

9. Ergonul O, Celikbaş A, Tezeren D, Guvener E, Dokuzoğuz B. Analysis of risk factors for laboratory-acquired brucella infections. J Hosp Infect. 2004 Mar;56(3):223-7. doi: 10.1016/j.jhin.2003.12.020

10. Hsu CH, Farland J, Winters T, Gunn J, Caron D, Evans J. Laboratory-acquired vaccinia virus infection in a recently immunized person--Massachusetts, 2013. MMWR Morb Mortal Wkly Rep. 2015 May 1;64(16):435-8.

11. Kortepeter MG, Martin JW, Rusnak JM, Cieslak TJ, Warfield KL, Anderson EL, et al. Managing potential laboratory exposure to ebola virus by using a patient biocontainment care unit. Emerg Infect Dis. 2008 Jun;14(6):881-7. doi: 10.3201/ eid1406.071489

12. Lim PL, Kurup A, Gopalakrishna G, Chan KP, Wong CW, Ng LC, et al. Laboratory- acquired severe acute respiratory syndrome. N Engl J Med. 2004 Apr 22;350(17): 1740-5. doi: 10.1056/NEJMoa032565

13. International health regulations (2005). Third edition. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/bitstream/handle/10665/246107/9789241580496-eng.pdf?sequence=1, accessed 6 December 2019).

14. Biosafety and biosecurity: standard for managing biological risk in the veterinary laboratory and animal facilities. In: Manual of diagnostic tests and vaccines for

terrestrial animals, 8th edition. Paris: World Organisation for Animal Health (OIE); 2018 (https://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/1.01.04_BIOSAFETY_BIOSECURITY.pdf, accessed 6 December 2019).

15. Biorisk management. Laboratory biosafety Guidance. Geneva: World Health Organization; 2006 (https://www.who.int/csr/resources/publicatio ns/biosafety/WHO_CDS_EPR_2006_6.pdf, accessed 6 December 2019).

16. WHO Global Plan of Action on Workers' Health (2008-2017): Baseline for Implementation. Geneva: World Health Organization; 2007 (https://www.who.int/occupational_health/who_workers_health_web.pdf, accessed 6 December 2019).

17. Biosafety program management. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs)

18. Risk assessment. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

19. Biological safety cabinets and other primary containment devices. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

20. Personal protective equipment. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

21. Laboratory design and maintenance. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

22. Decontamination and waste management. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

23. Outbreak preparedness and resilience. Geneva: World Health Organization; 2020 (Laboratory biosafety manual, fourth edition and associated monographs).

24. The International Federation of Biosafety Associations Laboratory biosafety and biosecurity risk assessment technical guidance document. Albuquerque: Sandia National Laboratories; 2014 (https://prod-ng.sandia.gov/techlib-noauth/access-control.cgi/2014/1415939r.pdf, accessed 6 December 2019).

25. Responsible life sciences research for global health security. Geneva: World Health Organization; 2010 (https://apps.who.int/iris/bitstream/handle/10665/70507/ WHO_HSE_GAR_BDP_2010.2_eng.pdf?sequence=1, accessed 6 December 2019).

26. Renn O. White Paper on risk governance: toward an integrative framework. In: Renn O, Walker KD, editors. Global risk governance. Dordrecht: International Risk Governance Council; 2008. doi:10.1007/978-1-4020-6799-0_1.

27. Laboratory safety guidance. Washington, DC: Occupational Safety and Health Administration, US Department of Labor; 2011 (https://www.osha.gov/Publications/ laboratory/OSHA3404laboratory-safety-guidance.pdf, accessed 6 December 2019).

28. Pedrosa BS, Cardoso, TA. Viral infections in workers in hospital and research laboratory settings: a comparative review of infection modes and respective

biosafety aspects. Int J Infect Dis. 2011 Jun;15(6):e366-76. doi: 10.1016/j.ijid.2011.03.005

29. Siengsanan-Lamont J, Blacksell SD. A review of laboratory-acquired infections in the asia-pacific: understanding risk and the need for improved biosafety for veterinary and zoonotic diseases. Trop Med Infect Dis. 2018 Mar 26;3(2):36. doi: 10.3390/tropicalmed3020036

30. Kimman TG, Smit E, Klein, MR. Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures. Clin Microbiol Rev. 2008 Jul;21(3):403-25. doi: 10.1128/CMR.00014-08

31. Baldwin CL, Runkle RS. Biohazards symbol: development of a biological hazards warning signal. Science. 1967 Oct 13;158(3798):264-5. doi: 10.1126 science. 158.3798.264

32. United Nations. Recommendations on the transport of dangerous goods: model regulations, 21st revised edition. New York, Geneva: United Nations; 2019 (https:// www.unece.org/trans/danger/publi/unrec/rev21/21files_e.html, accessed 13 November 2020).

33. Technical instructions for the safe transport of dangerous goods by air (Doc 9284), 2017-2018 edition. Montreal: International Civil Aviation Organization; 2017 (https:/ www.icao.int/safety/DangerousGoods/AddendumCorrigendum%20to%20the%20 Technical%20Instructions/Doc%209284-2017-2018.AddendumNo2.en.pdf, accessed 6 December 2019).

34. Infectious substances shipping guidelines, 15th edition (2019/2020). Montreal, International Air Transport Association; 2019

35. IMDG code. International maritime dangerous goods code: incorporating amendment 39-18. 2018 edition. London: International Maritime Organization; 2018 (http://www.imo.org/en/Publications/IMDGCode/Pages/Default.aspx, accessed 6 December 2019).

36. ADR, applicable as from 1 January 2019. European agreement concerning the international carriage of dangerous goods by road, Volumes I and II. New York and Geneva: United Nations; 2019. (http://www.unece.org/trans/danger/publi/adr/ adr2019/19contentse.html, accessed 6 December 2019).

37. Regulation concerning the international carriage of dangerous goods by rail (RID). Berne: Intergovernmental Organisation for International Carriage by Rail; 2019. (https://otif.org/en/?page_id=1105, accessed 6 December 2019).

38. Nagoya protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilization to the convention on biological diversity. Montreal: Secretariat of the Convention on Biological Diversity; 2014 (https://www. cbd.int/abs/doc/protocol/nagoya-protocol-en.pdf, accessed 6 December 2019).

39. Guidance on regulations for the transport of infectious substances 2019-2020. Geneva: World Health Organization; 2019 (WHO/WHE/CPI/2019.20) (https:// apps.who.int/iris/bitstream/handle/10665/325884/WHO-WHE-CPI-2019.20-eng. pdf?ua=1, accessed 6 December 2019).

40. Biorisk management. Laboratory biosecurity guidance. Geneva: World Health Organization; 2006 (https://www.who.int/csr/resources/publications/biosafety/WHO_CDS_EPR_2006_6.pdf, accessed 6 December 2019).

41. WHO guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories – a stepwise approach. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/bitstream/handle/10665/332244/9789241516266-eng.pdf?sequence=1&isAllowed=y, accessed 15 June 2020)

42. An analytical approach: biosafety and biosecurity oversight framework [e-learning course]. Government of Canada; 2020 (https://www.canada.ca/en/public-health/ services/laboratory-biosafety-biosecurity/analytical-approach.html, accessed 20 April 2020 [subscription required])

43. The Biological Weapons Convention. Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction. United Nations; 1975 (https://www.un.org/ disarmament/wmd/bio/, accessed 6 December 2019).

44. International Organization for Standardization (ISO) [website] (https://www.iso. org/home.html, accessed 6 December 2019).

45. Biosafety in microbiological and biomedical laboratories, 5th edition. Washington, DC: US Department of Health and Human Services; 2009 (https://www.cdc.gov/labs/pdf/CDC-biosafetyMicrobiologicalBiomedicalLaboratories-2009-P.PDF, accessed 6 December 2019).

Further information

Biological safety cabinet (BSC) 1: Introduction [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/KHCT9OJqxPo, accessed 6 December 2019).

Biological safety cabinet (BSC) 2: Preparatory steps [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/4DoHJS8JL4U, accessed 6 December 2019).

Biological safety cabinet (BSC) 3: Best practices for safe usage [Biosafety video series]. Geneva: World Health Organization; 2019 (https://www.youtube.com/ watch?v=18QEJUA9XBs, accessed 6 December 2019).

Biological safety cabinet (BSC) 4: Incident management [Biosafety video series]. Geneva: World Health Organization; 2019 (https://www.youtube.com/watch?v=aS_ TCZTCcsI, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 1: personal protective equipment (PPE) [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/Cuw8fqhwDZA, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 2: pipettes [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/-zeCI8ESrpU, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 3: sharps [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/yqX8hhzX7xU, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 4: surface decontamination [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/ b0PtPEnNakc, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 5: autoclaves [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/Yfc1yjEuuhE, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 6: workflow [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/TeYA2KqIU5k, accessed 6 December 2019).

Good microbiological practices and procedures (GMPP) 7: transport [Biosafety video series]. Geneva: World Health Organization; 2019 (https://youtu.be/RC9QHf2wdX0, accessed 6 December 2019).