

CHAPTER 1.1.4.

BIOSAFETY AND BIOSECURITY: STANDARD FOR MANAGING BIOLOGICAL RISK IN THE VETERINARY LABORATORY AND ANIMAL FACILITIES

INTRODUCTION

Chapter 1.1.1 Management of Veterinary Laboratories outlines the overall requirements and responsibilities to be addressed in the management of veterinary laboratories, of which management of the biological risks associated with the operation of a laboratory is an important aspect. This chapter outlines the principles on which the specific management of biological risks associated with veterinary laboratories and experimental animal handling facilities should be based. The terminology is aligned with the OIE nomenclature for risk analysis, including the four components, namely hazard identification, risk assessment, risk management and risk communication, used in Chapter 2.1 Import Risk Analysis of both the OIE Terrestrial Animal Health Code and OIE Aquatic Animal Health Code. In this way the process is consistent with and standardised against risk analysis processes already used by OIE Member Countries.

Adoption of the risk analysis approach to management of biological risks for biosafety and biosecurity in veterinary laboratories and animal facilities provides Member Countries with a means of tailoring their relevant national animal health policies and procedures regarding their laboratories to their particular circumstances and priorities. The biological risk management approach gives countries a mechanism to protect their human and animal populations from inadvertent or intentional release of or exposure to animal pathogens in an evidence-based, transparent, economically viable and sustainable manner. The approach is applicable in all countries from technologically advanced to in-transition or resource-limited countries.

The risk analysis approach moves towards a comprehensive biological risk management framework that is science-based and specific to an individual country and laboratory's circumstances. The process could accommodate the assigning of pathogens to risk groups relevant to the country and the subsequent restriction of the associated work to laboratory facilities defined by containment levels tailored to the types of risk identified if this suits an individual country's requirements as identified by its biological risk analysis. This chapter and the associated Chapter 3.5 Managing biorisk: examples of aligning risk management strategies with assessed biorisks provide the framework for implementation of the risk management approach.

Veterinary laboratories and animal facilities routinely handle biological materials that may constitute or contain infectious agents and toxins that may cause adverse animal or public health and economic effects due to uncontrolled release inside or outside the laboratory. Laboratory and animal facilities managers are responsible for providing a management system that ensures safe and secure handling, storage, and transport of these biological materials (a biological risk management system). This is needed not only to protect laboratory workers from inadvertent exposures and infection, but also to protect the local and regional animal populations, human populations, and environment from accidental or intentional release and spread of biological agents and toxins from laboratories. These considerations should also apply to animals and potential arthropod vectors that are handled in veterinary laboratories and animal facilities. The term "biological material" is used throughout this chapter to include all potential sources of biological risk for which laboratory management may be responsible. To classify the potential biological risk posed by the presence and handling of a particular biological material, laboratory managers should apply a systematic and evidence-based approach.

Biological risk analysis is the process of identifying and characterising health, safety, and security risks, followed by implementing, measuring the effectiveness of, and communicating the control measures used to reduce those risks to acceptable levels. Risk analysis has been used effectively by individuals in business and finance, engineering, energy, and health industries to characterise and control inherent risks associated with their business practices. This chapter focuses on biological-related risks, recognising that additional health and safety concerns exist, and should be controlled within the laboratory environment, such as radiation exposures, chemical burns, or liquid nitrogen hazards. A laboratory biological risk management system includes the policies, responsibilities, and operational procedures used to support biological risk analysis and the resulting biosafety and laboratory biosecurity measures implemented to manage laboratory biological risks.

Additional definitions and further explanation of the risk analysis principles and associated laboratory biological risk management system approach presented in this chapter can be found in the OIE Handbook on Import Risk Analysis for Animals and Animal Products and in the European Committee for Standardization (CEN) Workshop Agreement on Laboratory Biorisk Management. Following the overview presented in this chapter, a general guide for performing a risk analysis is included in Appendix 1.1.4.1. The types of biological hazards to be considered, the associated risks and the types of management strategies to be considered are provided in a table in Appendix 1.1.4.2. Chapter 3.5 contains worked examples based on hypothetical scenarios of how the checklist can be worked through for specific infectious hazards.

A. LABORATORY BIOSAFETY AND BIOSECURITY BACKGROUND

As outlined in Chapter 1.1.1 *Management of Veterinary Laboratories*, it is a standard for Member Countries having such facilities that they be managed within the context of a formally stated animal health policy that indicates clearly the purposes for which laboratory services are required. This animal health policy typically includes specific mention of the disease agents for which a diagnostic or research capability is required and allows for the subsequent design and development of a laboratory capability that is fit for purpose. The design of the laboratory capability will guide decisions regarding the use or avoidance of particular direct and indirect laboratory test methods that may involve the handling, propagation, and storage of particular infectious agents or toxins in the laboratory. This process should be expected to result in a list of the biological materials, including each specific infectious agent that will be held by the laboratory.

Biological risk assessments are undertaken to inform and determine the policy and procedures that in turn give confidence that the laboratory procedures for each of the biological materials handled by the laboratory pose negligible danger to a country's animal and human populations. The assessments of biological risk are usually taken at a national or jurisdictional level and may lead to national or jurisdictional standards or regulations for biological risk management that are followed by all veterinary laboratories and animal handling facilities in that country or jurisdiction. Agencies and laboratories responsible for biological risk analysis may make use of data, information and guidance available in published technical documents such as specific chapters of the OIE *Terrestrial Animal Health Code*, the *Aquatic Animal Health Code* and this *Terrestrial Manual* as well as publications from other internationally recognised bodies and organisations.

It is the intention of this chapter to provide countries and laboratories with a process that can be applied when developing standards, policies and procedures appropriate to their particular circumstances. It is additionally a requirement that the process be transparent to other Member Countries that may have a legitimate interest in the effectiveness of the management of laboratory biological risks in the particular country. Although this chapter is applicable to veterinary laboratories and animal handling facilities, it is noted that in the international context, issues that have an impact on public health are also subject to binding international agreement. Consequently, the veterinary biological risk analysis process must deliver outcomes in support of the particular country's obligations regarding zoonotic diseases, such as under the World Health Organization (WHO) International Health Regulations (IHR) (WHO, 2005). For countries in the process of developing their national standard, this chapter provides guidance for identifying and assessing the country's animal health risks and related laboratory management strategies.

Laboratory biosafety describes the principles and practices for the prevention of unintentional release of or accidental exposure to biological agents and toxins. Laboratory biosecurity describes the physical control of biological agents and toxins within laboratories, in order to prevent their loss, theft, misuse, unauthorised access or intentional unauthorised release. These and other terms are defined in the Glossary of this *Terrestrial Manual*.

Laboratory risk assessments are used to identify the specific biosafety and biosecurity measures needed to contain and work safely with specific biological agents and toxins in a laboratory or animal facility. The common practice of linking a biological agent to a specific level of biocontainment arises from the concept of identifying biological agents and toxins as *biohazards* and classifying the individual agents into one of four risk groups based on the potential to cause disease in an individual and in a community. The criteria used in risk group classification schemes, which although similar are not consistent between countries, typically include pathogenicity, mode of transmission, host range, the presence of vectors, existing levels of population immunity, availability of appropriate prophylaxis or treatment, density and movement of the host population, and related environmental factors.

Independent of the biological agent “risk group” classification process, biosafety level designations (alternately termed physical containment levels) were historically developed to characterise laboratories based on a composite of physical design features, facility construction, equipment, operational procedures, and laboratory practices required for working safely with the range of biological agents and toxins that pose varying levels of risk to individuals and to a community. Laboratory facilities have been designated by WHO as: basic – Biosafety Level (BSL) 1 (basic teaching and research); basic – BSL 2 (primary health services, diagnostics, research); containment – BSL 3 (special diagnostics, research); and maximum containment – BSL 4 (dangerous pathogens) (WHO, 2004). The biosafety level classification system has been questioned in that uniform standards and definitions are not used globally, therefore comparison of laboratories using the numerically designated classification schemes of different countries may not be equivalent or representative.

It is critical to note that the classification of specific biological agents into risk groups was never intended to equate directly with similarly designated laboratory biosafety levels; instead, the link between a specific agent and specific individual biosafety measures was intended to be determined by an assessment of biological risk associated with the presence and handling of the individual biological agent and the associated procedures used in the particular facility or environment. It is the individual biosafety and laboratory biosecurity measure or composite of measures, rather than a designated biosafety level, that guides a laboratory in the safe and secure handling of any individual biological agent or toxin. These specific biosafety and biosecurity measures are identified during a *biological risk assessment* which takes into consideration a laboratory’s organisation, the facility, and the surrounding environment in which the biological agent or toxin is to be handled. Over time the role of formal risk assessments in selecting appropriate biological risk mitigation measures has been minimised or over-looked in many laboratories, and replaced by generic assignment of biological agents based on their risk group classification into laboratory facilities defined by one of the four biocontainment levels. Such practices do not necessarily lead to appropriate strategies for the informed management of biological risks.

Moreover the expense of building and of maintaining high level containment laboratories can be impractical or prohibitive for some countries, or may simply not provide the most practical and feasible means of managing a specific biological risk. A laboratory-specific biological risk assessment and associated laboratory risk control decisions based on the country or region’s animal health strategy, including consideration of endemic disease status, environment, animal movement, trade arrangements, and geopolitical borders, tends to be both more practical and effective.

This chapter defines the terminology and approaches used in biological risk analysis, and in doing so provides a practical approach for countries, jurisdictions and veterinary laboratories to develop, implement, and maintain appropriate biosafety and laboratory biosecurity measures leading to a functional and efficient biological risk management system.

B. BIOLOGICAL RISK ANALYSIS AND BIOLOGICAL RISK MANAGEMENT SYSTEM

Biological risk analysis includes identification of biohazards, a laboratory assessment followed by management of the associated biological risks, and biological risk communication. For veterinary laboratories, biological risk analyses focus on the potential for animal, human, and environmental exposures, including both intentional and unintentional release of biological agents and toxins from the laboratory. It is the laboratory’s biological risk management system that ultimately provides laboratory managers, as well as the veterinary authorities of a country or jurisdiction, with a structured process for assessing, reviewing and controlling biological risks.

The laboratory’s biological risk management system includes the policies, procedures, and operational components needed for identifying, determining the extent of, managing, and communicating disease and economic risks associated with a specific biological agent in the context of how that agent is handled, manipulated, and maintained in the laboratory.

It is the responsibility of the laboratory to ensure suitable methodologies for the allocation of actions resulting from biological risk assessments, including timelines, responsible persons, and that the associated reporting and approval mechanisms are identified, implemented, and maintained (CEN, 2011). This is accomplished through

the development of a risk management policy appropriate to the nature and scale of the facility, activities, and associated biological risks. The policy (or policies) is designed to (a) protect staff, contractors, visitors, the community, surrounding animal populations, and the environment from unintentional or intentional release of or exposure to biological agents and toxins stored or handled within the facility; (b) reduce to acceptable levels laboratory risks that may result in release of or exposure to biological agents by conducting risk assessments of laboratory facilities and work practices, identifying appropriate risk control measures, implementing, and monitoring those measures for effectiveness; and (c) effectively informing and communicating to employees and relevant stakeholders the findings and obligations of the risk management system.

A successful biological risk management system will have clear and unequivocal commitment by laboratory management, who ensure that roles, responsibilities, and authorities related to biological risk management are defined, documented, and communicated to those who manage, perform, and verify work associated with biological agents and toxins in the laboratory. Laboratory management will ensure (a) the provision of adequate resources; (b) prioritisation and communication of biosafety and biosecurity policy; (c) integration of biosafety and biosecurity practices throughout the laboratory; and (d) a robust process of monitoring and evaluation that identifies opportunities for improvement, determines root causes where unsatisfactory situations arise and revises policies and procedures to prevent recurrence. The ongoing verification and continual improvement of a laboratory's effectiveness in managing its risks is a key component of a complete and effective biological risk management system.

Each laboratory should appoint a biological risk management advisor who will report directly to senior laboratory management and have authority to lead the development and implementation of the biological risk management system, be responsible for developing and maintaining documentation for all aspects of the system, and for monitoring the system within the laboratory or facility. The biological risk management advisor is an individual knowledgeable about the laboratory facility, laboratory procedures used, and biological agents and toxins likely to be encountered in the particular laboratory. In smaller laboratories the biological risk management advisor may also have other roles or duties, often quality management or safety management. The designated biological risk management advisor will have the authority delegated from senior management to call for the cessation of work that is not compliant with the laboratory's biological risk policies and procedures.

The key functions of biological risk analysis are: (a) biohazard identification (i.e. what can go wrong?); (b) biological risk assessment (i.e. how likely is the hazardous event to occur and how severe would be the harm?); (c) risk management (i.e. how can those risks be prevented or minimised to acceptable levels?); and (d) risk communication (i.e. how was the risk identified, characterised and controlled?). In addition there is a need for (e) verification with continual improvement (i.e. are the biosafety and laboratory biosecurity measures effective in controlling the biological risk and can they be improved?). The organisational structure, responsibilities, policies, and practices that provide for these activities, comprise a laboratory's biological risk management system. It is important that all relevant regulatory requirements are identified and fulfilled within the biological risk management system. Legal requirements include any national, federal, regional, state, provincial, city and local regulations with which the laboratory is obliged to comply.

1. Biohazard identification

The first step in the risk analysis process is identifying and documenting the potential laboratory biohazard(s). A *biohazard* can be any biological agent, toxin, or associated laboratory or animal facility procedure with the potential for causing harm or damage. During the biohazard identification process, it is necessary to identify biological agent characteristics that make the agent hazardous, and potentially make the agent attractive for malicious use or theft. Although not the focus of this chapter, it should additionally be noted that laboratories must be critically aware of all potential hazards (any source, situation, or act with the potential for causing harm) in the laboratory environment, and not just those that are specifically biological in nature. Examples would include electrical safety, physical safety or radiation hazards, and issues relating to utility failure, poor training, selection of suppliers, etc. that may not appear directly to link themselves to the biological agents and toxins, but that can result in release of a biological agent or toxin, as well as causing other harm.

A laboratory's risk management system should be complete in identifying and managing all hazards, including those outlined hereafter.

1.1. The inventory of biological materials held by and/or manipulated by the laboratory

All biological materials held by the laboratory must be known, recorded and individually addressed in the biological risk assessment process. The specific agents and toxins that a laboratory works with and the associated technical procedures used in that work must be recognised. This will be the primary focus of the biological risk assessment.

1.2. Diagnostic specimens

Veterinary diagnostic centres routinely receive specimens that have been submitted because they are suspect for any of a variety of diseases. While the infectious nature of the specimens is unknown, diagnostic case materials may contain a variety of unknown agents, some of which could be extremely hazardous to human health or pose a significant threat to animal populations. Veterinary diagnostic laboratories have the responsibility to implement appropriate biosafety and laboratory biosecurity measures to minimise the risk of occupational exposure of employees, or of release and spread to the population of pathogens that may be contained within diagnostic specimens. Initial laboratory processing of all unknown diagnostic specimens must be carried out with the assumption that an infectious agent or toxin likely exists in the specimens submitted. Until the specimen has been characterised as non-infectious, it is important that veterinary laboratories take adequate precautions to prevent exposure via percutaneous and mucous membrane routes, and particularly through inhalation and ingestion. Once a specific agent or toxin has been identified by the laboratory, further work is carried out using relevant biocontainment and risk controls.

1.3. Transportation and storage of pathogens

Requirements used for the safe and secure transportation of specimens are given in Chapter 1.1.3 *Transport of specimens of animal origin*. Storage of viable agents is a common laboratory and animal facility practice, and therefore a biohazard, in most if not all veterinary laboratories and animal facilities. The risks associated with accidental contact or unauthorised access to biological agents and toxins must be addressed within the storage facility and inventory system. As noted previously, it is an important biosecurity responsibility of veterinary laboratories and animal facilities to identify and to minimise any risk of release of pathogens into human and animal populations, either domestic or wild.

1.4. Physical and chemical hazards

Physical and chemical hazards associated with routine laboratory and animal-use manipulations cannot be ignored during biohazard identification exercises. The laboratory and animal facility must identify these hazards within their facility in order to ensure that their biosafety programmes adequately protect laboratory workers. Examples of hazards routinely found in veterinary laboratories include handling and disposal of glass, needles, and sharp instruments; burns from hot solids, liquids, or from radiation, and burns and asphyxiation risks associated with liquid nitrogen; explosion risks associated with incorrect or non-compatible storage of chemicals; and exposure or repeated exposure (dose-effect) to mutagenic, carcinogenic, and toxic chemicals through respiratory and percutaneous routes.

1.5. Laboratory animals

Work with laboratory animals is also an important laboratory hazard. Laboratory animals can generate large amounts of infectious agent, as well as pose risks associated with the potential for bites, scratches, kicks, and related injury to care-takers and laboratory workers. Expanded information on health and safety in laboratory animal facilities is available (Wood & Smith, 1999).

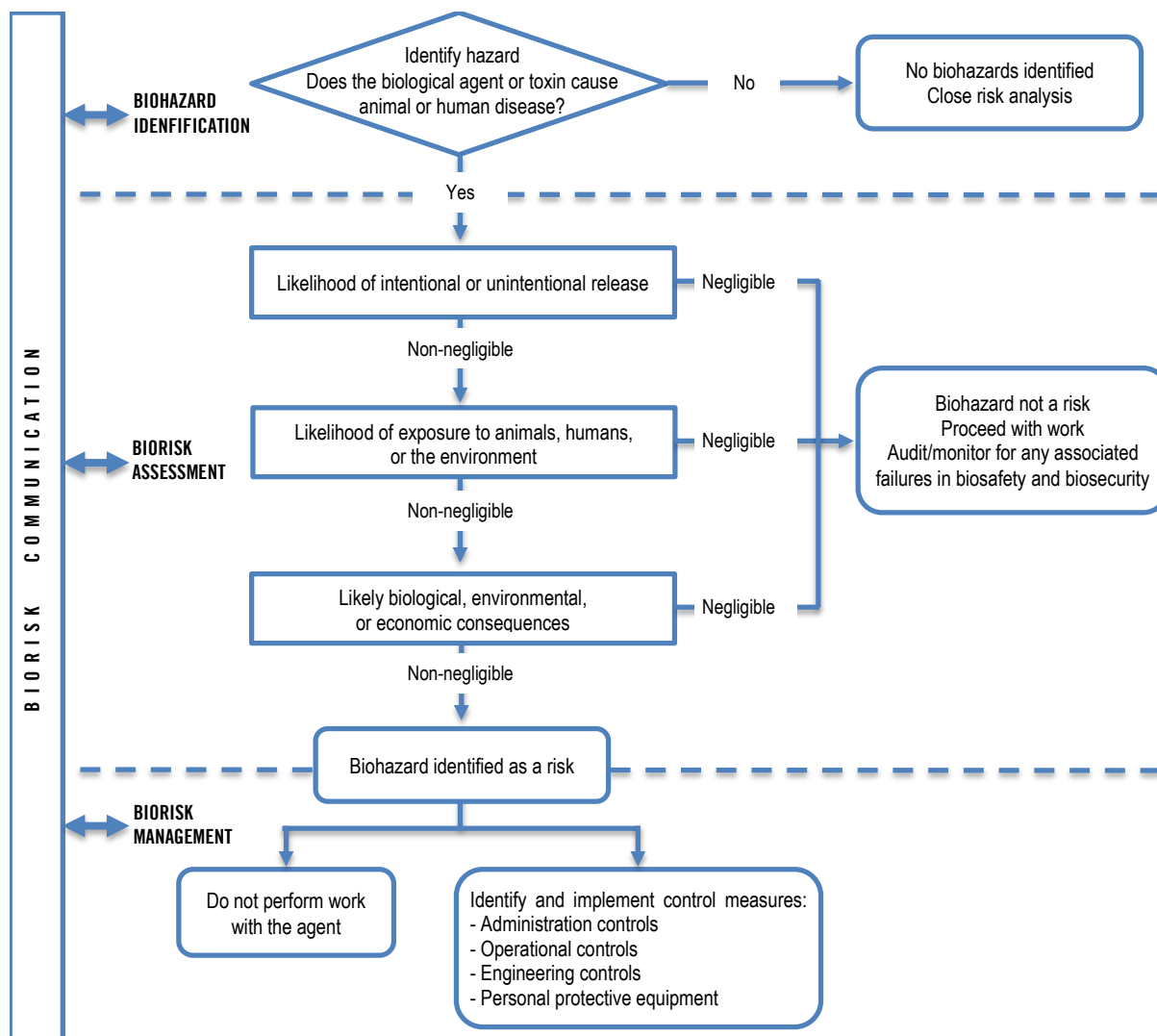
2. Biological risk assessment

The laboratory's approach to biological risk assessment is a component of the laboratory's risk management policy that defines the scope, nature, and timing of assessments so that the process is proactive rather than reactive. Following identification of the biohazard, the next step in the biological risk assessment process is determining the likelihood and potential severity of consequences or harm associated with that biohazard. Severity (or harm) can be thought of as the biological, environmental, and economic impacts associated with a release of and exposure to the biohazard. The severity of harm associated with animal pathogens and toxins will include human and animal disease, as well as economic losses associated with local, national, regional, and international restrictions on animal movement and on commerce associated with animals and animal products.

Risk is defined as a combination of the likelihood (probability) of the occurrence and the severity of harm (or consequence); the term biological risk is used where the source of harm is a biological agent or toxin. At this point in the biological risk analysis process (see Flowchart 1), the laboratory with the assistance of their biological risk management advisor, will evaluate the individual facility, human resources, protocols, methodologies and procedures to determine how the biohazard is to be handled and manipulated in their specific circumstances; in addition to assessing the surrounding environment, including identifying susceptible species and the specifics of the biological agent's transmission in order to determine the likelihood and severity of harm (see Table A).

A comprehensive biological risk assessment includes evaluation of both biosafety and laboratory biosecurity practices. Biosafety addresses risks associated with exposure to, or accidental release of the biological material, while laboratory biosecurity addresses potential for theft, misuse, or deliberate release. A comprehensive risk assessment would include consideration of all relevant items that could be at risk for theft or misuse (e.g. electronics, computers, balances) that make the facility a target for theft. It is necessary to consider both biosafety and laboratory biosecurity to ensure that risk control measures implemented are not in conflict with each other and that any one control measure does not compromise others.

Flowchart 1: Biological risk analysis process



Note: The biological risk management process should address all laboratory processes and procedures associated with the specific hazard (biological agent or toxin). The biological risk assessment and biological risk control planning involves a team of individuals who understand the organisational aspects of the laboratory, the biology and pathogenesis of the agent, and the impacts of exposures and accidental or intentional release of the biological agent or toxin.

The biological risk assessment may be quantitative, using mathematical models (OIE, 2010b), or may be qualitative (CEN, 2011; OIE, 2010a). For the qualitative biological risk assessment approach discussed here, both likelihood and severity are given a non-numerical score or ranking, which allows a form of “quantifying” the biological risk by using qualitative definitions such as low, moderate, and severe or other non-numerical equivalents. The rankings determined for likelihood and severity of harm will help the laboratory further characterise its biological risks in order to determine the biosafety and laboratory biosecurity control measure(s), the necessary redundancy in controls, and the overall financial investment that will be appropriate to mitigate their specific biological risks.

Resource utilisation and financial investments in biological risk control measures should be proportionate to the biological risks identified in the assessment process (‘protect pencils like pencils and diamonds like diamonds’). For example, one outcome of biological risk assessment is a very low likelihood score (e.g. unintentional release

of the agent from laboratory containment via some specified process, such as waste treatment), with an extremely high severity score (e.g. release of a non-endemic biological agent with high transmissibility paired with high morbidity or mortality in a susceptible population, loss of trade status, and severe social and economic impacts). In such a case, the laboratory may determine that there are no available mitigation or combination of biosafety and biosecurity measures that would be sufficient to justify handling the biological agent in their facility. The same scenario occurring in a country or region where the agent is endemic may result in the same likelihood ranking, but carry a significantly lower severity ranking. This country could justify an investment for determining and then implementing appropriate biosafety and laboratory biosecurity measures to decrease the likelihood of an unintentional release to an acceptable minimum level.

Where it is determined for a specific biological agent or toxin that there is no severity of harm associated with exposure or release, the biological risk assessment can be concluded.

3. Biological risk management

Where the biological risk assessment identifies unacceptable biological risks, the laboratory is responsible for responding by not handling or storing the specified agent in its facility (elimination of the hazard); by using alternative technical procedures (substitution); or by identifying, implementing and maintaining appropriate biosafety and laboratory biosecurity measures. The response to a biological risk assessment requires documentation of the timelines for action, assignment of responsible persons, and the associated reporting and approvals. Dependent on the outcome of the biological risk assessment (likelihood and severity rankings), the laboratory managers working with the biological risk management advisor will identify which biosafety and biosecurity measure(s) are appropriate and feasible for use within the laboratory or animal facility in order to prevent release of and exposure to the biohazard. The principal routes for exposure and release of biological agents and toxins from laboratory environments include:

- i) personnel via surface contamination, infection, or intentional acts allowing release;
- ii) aerosol;
- iii) liquid and solid waste;
- iv) equipment and materials;
- v) specimens and reagents;
- vi) release via research animals or disease vectors.

To protect biological agents and toxins from unauthorised access or use, the laboratory should additionally consider laboratory security. In general, the components of laboratory security include

- i) physical security (e.g. building structure, lockable doors);
- ii) personnel (including steps taken to ensure an employee does not pose a safety or security risk);
- iii) material control and accountability (inventory control and storage records);
- iv) information and information technology security;
- v) security of materials during transportation (ensuring the biological material is not subject to theft or diversion during transportation within a facility or between facilities).

In the absence of elimination or substitution as a possible risk control strategy, a strategy that includes administrative, operational, engineering, and personal protective equipment (PPE) controls is used to prevent exposures and accidental or intentional release. The different control approaches are complementary and are used in combination to accomplish appropriate risk reduction. A most basic biosafety and biosecurity programme will ultimately require implementation, at varying degrees, of all the different types of control strategies.

- i) *Administrative controls*: qualified and suitable personnel; training and verification of competency of staff in the safe and secure handling of biological agents and toxins, in applicable technical procedures, and in use of PPE and equipment; health and safety programmes; prophylactic health care including vaccinations; emergency response and contingency plans; incident and accident investigation programmes; current biological agents and toxin inventory and inventory management requirements including access, storage, transfer, destruction, and audit; waste management policies; and security policies including facility security, visitor access, personnel security, access to biological agents and toxins; and information security.
- ii) *Operational controls*: Standard Operating Procedures for all safety and laboratory biosecurity-relevant processes including Good Microbiological Technique (GMT); disinfection and decontamination practices; transport procedures; general laboratory safety; specimen and reagent handling and storage practices; waste management practices including disinfection and inactivation; emergency exercise drills; and accident/incident reporting, response, and review protocols.
- iii) *Engineering controls*: physical features of the facility including ventilation and air-flow, barrier walls and shields, and separation of incompatible activities; equipment and equipment maintenance, calibration and certification; and physical security such as access restrictions, perimeter fences, facility and equipment locks

with key control protocols, badge readers, detectors and sensors, or biometric devices. The laboratory must have measures to ensure that all changes to the facility associated with design, operation, and maintenance are documented and that documentation is used to update prior biological risk assessments that may be affected by the change. Engineering controls include the following principles of containment:

- a) *Primary containment layers* are those that enclose the biological agent or toxin within sealed containers or in a Class I, II or III biosafety cabinet. Biological biosafety cabinets must be installed and certified in accordance with the national or manufacturer's standards to ensure effective functioning. Class I cabinets provide personnel and environmental protection. The contents of Class I cabinets are not protected from environmental contamination. Class II cabinets draw a curtain of sterile air over the contents of the cabinet and exhaust through high efficiency particulate air (HEPA) filters in order to protect the contents of the cabinet, personnel, and the environment. Class III cabinets are gas-tight and designed for maximum containment. Class III cabinet engineering (e.g. attached gloves, dunk tanks, etc.) and protocols for use prevent direct contact with hazardous materials and air. In the case of infected animals, the agent is enclosed by physical containment in specially constructed rooms where all wastes are treated and air is filtered.
 - b) *Secondary containment layers* enclose infected materials and individuals working with infected materials within a closed and controlled physical environment that treats solids, fluids, and air using validated filtration and treatment procedures that remove or inactivate live agents.
 - c) *Tertiary containment layers* are those designed to prevent contact between biological agents and susceptible species using appropriate measures that physically restrict exposure to susceptible species.
- iv) PPE: body protection (i.e. clothing), hand protection (i.e. gloves), eye protection, and respiratory protection.

Laboratory biosafety should be based on a solid foundation of good microbiological practices in the laboratory to which all laboratory work conforms. The essential requirements for any work with infectious agents or specimens likely to contain infectious agents, however innocuous the material may seem, are as follows:

- i) The laboratory should be easy to clean, with surfaces that are impervious to water and resistant to chemicals used in the laboratory. There shall be a hand-wash basin, emergency shower, and eye wash station in each laboratory suite as appropriate for the chemicals and other hazards present. Procedures shall be established for frequent cleaning and disinfection of the work area during and at the end of the work period;
- ii) Personnel access to the work area should be restricted (security measures such as controlled access may be necessary with higher risk agents);
- iii) Basic PPE such as long-sleeved laboratory coats or gowns, closed-toe footwear, disposable gloves, and safety glasses, shall be worn in the laboratory and removed when leaving the laboratory. Masks, including face shields and oro-nasal respirators may be required as determined by the specific risk assessment;
- iv) The laboratory door should be closed when work is in progress, and appropriate access restriction, warning, or biosafety signage clearly visible;
- v) While forced ventilation is not a baseline requirement, appropriate ventilation shall be provided for the health and well-being of the workers and as required by risk assessment;
- vi) Food (including chewing gum, candy, throat lozenges and cough drops) and drinks shall not be stored or consumed in laboratories; smoking or application of cosmetics shall not take place in the laboratory;
- vii) Pipetting shall not be done by mouth;
- viii) Care shall be taken to minimise the production of aerosols;
- ix) Emergency response plans should be developed to deal with the biohazard of any safety or security incident. Items addressed in the plans should at a minimum include having effective disinfectants and instructions available for cleaning spills, removal and decontamination of contaminated protective clothing, washing of hands, and cleaning and disinfection of bench tops;
- x) Used laboratory glassware and other contaminated material shall be appropriately identified (labelled) and stored safely. Materials for disposal shall be transported without spillage in robust containers. Waste material should be autoclaved, incinerated or otherwise decontaminated or inactivated before disposal. Reusable material shall be decontaminated by appropriate means;
- xi) No infectious material shall be discarded down laboratory sinks or any other drain;
- xii) Any accidents or incidents shall be recorded and reviewed with the biological risk management advisor to assist in continually improving the biological risk management system;

xiii) Workers shall be appropriately trained and verified as competent to perform the tasks assigned.

The risk assessment process is used in determining the appropriate biosafety and laboratory biosecurity controls required for the biohazard (biological agent or toxin) and laboratory or animal facility procedure in question.

4. Risk communication

Laboratory risk communication is a continuation of hazard identification, risk assessment and risk management processes, and is an integral component of incident or outbreak preparedness and response planning. With the understanding that the laboratory's stakeholders and the public are entitled to information that impacts on their own health and the health of their animals, risk communications are designed to inform the laboratory's stakeholders about technical practices and decisions used for handling biohazards and for responding to incidents that may arise from release of and exposure to those biohazards. As laboratories handling animal pathogens and toxins are a critical component of a country or region's veterinary infrastructure, it is critical that the laboratory biological risk management process be thorough, objective, transparent, and clearly communicated (Covello & Allen, 1988).

Effective risk communication should be designed to establish a common understanding among the laboratory and associated stakeholders of the biological risks, biological risk control measures (biosafety and laboratory biosecurity practices implemented), as well as the benefits of working with the identified biohazard. This common understanding not only builds trust, but is critical for effectively responding to potential incidents and enabling impacted individuals and agencies to make informed decisions when working with the laboratory. Risk communication should be provided in a format and language that is tailored to the intended audience, whether policy-makers, disease control authorities, animal care providers, or the public, in order to provide the information in a clear and understandable manner. Effective biological risk communication requires that the complexities of technical language, scientific data, assumptions, and the justification for assumptions used in the biological risk assessment be fully documented.

In general, an initial laboratory biological risk communication is directed toward the appropriate health and disease control authorities and will identify; (1) the biohazard (biological agent or toxin); (2) the benefits to the stakeholder gained by the laboratory working with the biohazard; (3) information indicating that a biological risk analysis was performed and is documented; and (4) information indicating that the laboratory has biosafety and laboratory biosecurity measures in place to mitigate against accidental or intentional release of the biological agent or toxin.

In preparedness for of an accidental or intentional release of the agent, the laboratory should additionally be prepared for incident and incident response communication. Among the documents that the laboratory should generate prior to initiating work with a biohazard are (1) documentation of the roles and responsibilities of individuals involved in drafting, reviewing, approving, and distributing laboratory information and official communications, (2) a contact list containing the names, phone numbers, email addresses or other information as appropriate for those agencies and individuals to be notified, and (3) an incident response plan in the unlikely event of accidental or intentional release of the biological agent or toxin.

Contact lists should include (1) national, regional, and local disease control authorities (Veterinary Health and Public Health), as appropriate, (2) security authorities, as appropriate, for specific biothreat agents and risks, (3) the responsible physician or occupational health programme to be notified of human health-related agents, biological risks, and at-risk staff, and (4) stakeholders, including potentially impacted laboratory affiliates, e.g. shippers, rendering and waste disposal plants, janitorial staff, non-technical laboratory staff, potentially impacted local animal owners and industries.

5. Verification, corrective actions, and continual improvement

Biological risk management is an ongoing process in which specific biosafety and laboratory biosecurity measures are regularly monitored to ensure they are working as expected. The laboratory facility, management practices, and procedures should also be regularly reviewed to ensure that changes have not altered previously defined risks. Routine audits should be scheduled and conducted to document effectiveness of the implemented biosafety and laboratory biosecurity measures, to identify areas of noncompliance that need to be documented and corrected, and to identify areas for improvement. The process requires that the laboratory verify and document that the control measures implemented (e.g. administrative, operational, engineering, and PPE) effectively mitigate release of and exposure to the targeted biohazards. In a simple example: if during a laboratory assessment, the risk of release was defined as theft due to inadequate physical security, and the biosecurity control used was placement of a lock on the storage freezer, the laboratory administration would want to verify that the control implemented, locking the freezer, had mitigated the risk of theft. Assuming the administration found that the freezer key was kept on an accessible hook near the freezer, the risk of theft had not been adequately controlled and a corrective action would be implemented (e.g. additional or alternative choices of

biosecurity control measures, such as implementing added policy and procedures managing access to the freezer key).

It is the responsibility of laboratory managers to continually review and improve the laboratory's effectiveness through the use of documented policy and procedures, training of personnel and verification of competence, self-audit and external audit, where appropriate, corrective and preventive actions, and routine management reviews. The cycle of assessing biological risks, implementing control measures, verifying effectiveness, and correcting any weaknesses follows the same pattern used in well-functioning quality management programmes. Chapter 1.1.5 *Quality management in veterinary testing laboratories* provides an overview of the subject; the CEN Workshop Agreement on Laboratory Biological risk Management details the components of a comprehensive biological risk management system (CEN, 2011).

C. TECHNICAL GUIDANCE AND ASSESSMENT TOOLS

Technical advice and the level of detail needed for selecting individual laboratory and animal facility risk control measures is available through a number of published veterinary health and public health resources, including the WHO Biosafety Manual (WHO, 2004), CDC Biosafety in Microbiological and Biomedical Laboratories (CDC, 2009), Canadian Biosafety Standard and Guidelines (Government of Canada, 2013), Biological agents: Managing the risks in laboratories and healthcare premises (HSE, 2005), Laboratory Biosecurity Handbook (Salerno & Gaudioso, 2007), among others. Assessment tools such as the Food and Agriculture Organization of the United Nations (FAO) LMT (Laboratory Mapping Tool) and the Laboratory Assessment Checklists included in the WHO and CDC Biosafety Manuals, which are used for documenting a laboratory's capabilities and for monitoring compliance with laboratory management standards and good laboratory practices are additionally useful for both external and self-assessments.

D. CONCLUSION

The role of veterinary laboratories is to function as an integral component of a documented national animal health strategy to protect the health and well-being of local, national, regional, and global animal populations and associated commerce as well as protecting public health from biological risks of animal origin. The national animal health strategy will determine the biological materials, and particularly the infectious agents, for which the country's laboratories must maintain a capability.

Within the veterinary laboratory and animal facility environment there will be the inevitable presence and handling of biological materials that can pose biological risks for both animal and human populations. It is therefore of critical importance that laboratory and animal facility managers ensure that biological risks in their facility are clearly identified, understood, controlled, and communicated to the appropriate stakeholders. It is likely, and recommended, that these risks will be managed within the context of national regulations so that laboratory biological risk management strategies are consistent within countries. The standards communicated in this chapter apply to the development of national standards for managing the biological risks associated with laboratories as much as to the development of biological risk management systems within individual laboratories.

The discipline of biological risk analysis, paired with a comprehensive biological risk management system, allows those responsible to assess and document the laboratory biosafety and biosecurity practices which are used to provide appropriate controls, thus assuring adequate biosafety and laboratory biosecurity. A complete and functioning laboratory biological risk management system will help ensure that the laboratory is in compliance with applicable local, national, regional, and international standards and requirements for biosafety and laboratory biosecurity.

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APPENDIX 1.1.4.1.

STEPS IN BIOLOGICAL RISK ANALYSIS

1. Assemble a team for performing the risk assessment. Include individuals with knowledge and understanding of:
 - i) The physical and biological properties of the agent or toxin (e.g. the infectious dose, routes of infection, susceptible species, environmental survivability, etc.),
 - ii) The laboratory technologies and procedures to be used with the biological agent or toxin, associated technical competence, and laboratory facilities to be used,
 - iii) Laboratory biosafety and biosecurity practices,
 - iv) Risk analysis principles and practices.

One team member may serve multiple functions, and qualified individuals from outside of the laboratory performing the analysis may be used. The quality of the risk analysis performed is directly related to the level of knowledge and understanding provided by the team members.

2. Define the scope of the biological risk analysis
 - i) Biohazard Identification: identify the target biological agent or toxin. Perform a separate biological risk analysis for each relevant biological agent.
 - ii) Define the laboratory environment in which the biological agent or toxin will be used:
 - a) Identify technical procedures, methods and processes specifically to be used with the biological agent or toxin being evaluated (e.g. diagnostic specimens or reference materials, amplification in culture, centrifugation, ultrasound, pipetting, freeze–thaw, archival practices, concentrations and volumes of the biological agent or toxin, animal handling, etc.). These items define the laboratory environment relevant to the risk assessment, and document the potential sources of exposure and release from the laboratory environment.
 - b) Identify existing laboratory resources, including management and technical competencies (e.g. technical training and proficiency programmes, quality management practices, health and safety management programmes, etc.). These items document existing and potential sources of risk control.
 - c) Identify relevant laboratory facilities and associated resources (e.g. facility security, directional air-flow, autoclaves, incinerators, etc.). These items document existing and potential sources of risk control.
3. Develop and initiate the risk communication plan. The documentation and communication of risk analyses must be clear and complete. Because risk analysis supports decision-making where there is uncertainty in predicting events, it is critical that the process be transparent, objective, and clearly presented. It is useful to begin compiling the risk analysis report at the very beginning of the analysis in order to most effectively capture all relevant information, investigation, analysis, and findings.
4. Identify the severity of harm associated with any exposures or release of the biohazard from the laboratory. Severity should identify human health, animal health, and economic harm that would likely result from exposure and from release of the biological agent or toxin. Note that for a single agent, the economic cost of associated disease may vary considerably between a country in which the biological agent is endemic, and a country that is free of the biological agent. Where specific morbidity, mortality, and economic estimates are available, the source and context of the information must be provided. For example, existing risk analysis performed for import or export in association with a country or region may be used as a valuable source of economic data.

5. Perform the biological risk assessment, assigning a likelihood ranking and a severity ranking for agent release and for exposure to susceptible animals and humans for **each** laboratory procedure involving the biological agent or toxin in the laboratory (e.g. specimen receipt, necropsy, amplification in culture, centrifugation, nucleic acid extraction, storage, archive, animal experimentation, etc.) Biosafety assessments address the likelihood and severity of inadvertent exposure and of release of the biological agent. Biosecurity assessments address theft, loss, and intentional misuse of a biological agent.
6. Identify appropriate risk control measures available to the laboratory, including those biosafety and biosecurity measures already in place and those which could be implemented. There are often several different control measures that when used alone or in combination can provide equivalent results at similar or widely different costs. Each biosafety and laboratory biosecurity measure or combination of measures must be evaluated independently in order to determine the relative effectiveness in reducing the overall risk of exposure and release. It is the responsibility of the laboratory managers with the local, national, and regional disease control authorities to determine the economic and logistical feasibility of different control measures and appropriately balance the risks and benefits associated with the presence and handling of the biohazard.
7. Document the information and approach used in the risk assessment. The documentation must be complete, including data, methods of analysis, results, discussion, explanatory notes, and conclusions, dates and responsible personnel. References should be provided when relevant scientific and laboratory data and information is used (e.g. infectious dose, routes of transmission, working concentrations, environmental stability, etc.). All assumptions used must be identified and justifications for the assumptions must be provided.
8. Maintain or implement the selected biological risk control measures (biosafety and biosecurity practices) in the laboratory.
9. Make a record of and communicate the complete risk analysis, including implementation of the biosafety and biosecurity measures to the appropriate authorities and stakeholders. There are multiple report formats and templates available for documenting risk analysis. Examples can be found in the OIE *Handbook on Import Risk Analysis for Animals and Animal Products* (OIE, 2010a; 2010b) and in the *Seven Cardinal Rules of Risk Communication* (Covello & Allen, 1988).

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APPENDIX 1.1.4.2.

CONSIDERATIONS USED IN EVALUATING AND IMPLEMENTING BIOLOGICAL RISK CONTROL MEASURES

Chapter 3.5 Managing biorisk: examples of aligning risk management strategies with assessed biorisks provides illustrative examples of agent-specific risk assessments.

| Considerations used for identifying and assessing laboratory hazards | Determinant or level of risk for release from laboratory or exposure of staff | Examples of biological risk control measures |
|---|---|---|
| <p>Epidemiology of the biological agent; routes of transmission, including aerosol, direct contact, fomites, vectors; infectious dose, susceptible species, and likely extent of transmission.</p> <p>Origin of the agent outside the host.</p> | <p>Route(s) of transmission determines possible mechanisms for exposures or release from a laboratory.</p> <p>Origin of samples: specimens derived from wildlife may contain human or animal pathogens not normally encountered. Geographical source of specimens.</p> | <p>Different routes of transmission require specific mitigation measures:</p> <ul style="list-style-type: none"> - Aerosols: use of primary containment (e.g. biosafety cabinets), good microbiological technique (GMT), air filtration, directional airflow. -Surface contamination: disinfection, PPE including clothing and gloves, showering out of the laboratory. -Solid and liquid waste: waste treatment measures (e.g. autoclaving, chemical) -Fomites and materials exiting the laboratory: decontamination strategies |
| <p>May cause human or animal disease; <i>Severity of harm for laboratory workers, public health, and animal health.</i></p> | <p>Severe: potentially fatal disease, treatment or prophylaxis generally not available.</p> <p>Human: high individual or community risk.</p> <p>Animal: exotic or enzootic, subject to official control and that have high risk of spread from the laboratory into the environment and national/regional animal population.</p> | <p>Avoid release of the agent using a combination of administrative, operational, and engineering controls, and PPE. Considerations include stringent measures for biocontainment, decontamination and disinfection, redundancy of control measures used, GMT; mandatory training and competency for workers; mandatory employee health reporting programmes; mandatory laboratory security policies and procedures: redundancy of control measures, access control, due diligence in authorising personnel, inventory of seed and working stocks, intrusion detection, emergency response plans.</p> |
| | <p>Moderate: effective prophylaxis and treatments are generally available, but may be variable in effectiveness.</p> <p>Human: high individual risk, low community risk.</p> <p>Animal: exotic or enzootic, subject to official control and have moderate risk of spread from the laboratory.</p> | <p>Use a combination of administrative, operational, and engineering controls and PPE. Considerations include GMT such as effective infection control procedures, decontamination and disinfection, use of PPE and biosafety cabinets; employee health programmes (e.g. vaccination when relevant, health reporting); mandatory training and competency for workers; laboratory security policies and procedures. Access controls, escort for unauthorised individuals, inventory of seed stocks.</p> |

| Considerations used for identifying and assessing laboratory hazards | Determinant or level of risk for release from laboratory or exposure of staff | Examples of biological risk control measures |
|---|--|---|
| | <p>Low: effective prophylaxis and treatments are available.</p> <p>Human: moderate individual risk, low community risk.</p> <p>Animal: either exotic or enzootic, subject to official control and have low risk of spread from the laboratory.</p> <p>Human: no or low individual and population risk.</p> <p>Animal: enzootic, not subject to official control.</p> | <p>Considerations include routine use of GMT such as decontamination and disinfection, effective infection control procedures including use of dedicated laboratory clothing, biosafety cabinets; basic training and competency for workers. Waste management, including disinfection of laboratory wastes.</p> <p>Considerations include routine use of good microbiological practices (see Section B.3 of this chapter).</p> |
| <p>Impacts associated with animal population morbidity and mortality, and associated economic consequences (e.g. trade, food security, costs of disease control and movement controls, destocking or vaccination) dependent on whether the agent is exotic or endemic to the country or region.</p> | <p>Severe: Unacceptable costs nationally.</p> | <p>Avoid release of the biological agent using a combination of administrative, operational, and engineering controls, and PPE. Considerations include stringent biocontainment measures; specific features that are warranted by route(s) of exposure; PPE; GMT, decontamination and disinfection, primary containment systems; mandatory training and competency; mandatory laboratory security policies and procedures: redundancy of control measures, access control, due diligence in authorising personnel, inventory of seed and working stocks, intrusion detection, emergency response plans.</p> |
| | <p>Moderate: financial costs assessed on a case-by-case basis.</p> | <p>Use a combination of administrative, operational, and engineering controls, and PPE. Considerations include GMT such as decontamination and disinfection, effective infection control procedures including the use of PPE, and biosafety cabinets; air and effluent control; mandatory training and competency, laboratory security: access controls, escort for unauthorised individuals, inventory of seed stocks.</p> |
| | <p>Low: financial impact at manageable or existing levels.</p> | <p>Considerations include GMT such as decontamination and disinfection, effective infection control procedures including use of laboratory clothing and biosafety cabinets; basic training and competency.</p> |

| Considerations used for identifying and assessing laboratory hazards | Determinant or level of risk for release from laboratory or exposure of staff | Examples of biological risk control measures |
|--|---|--|
| <p>Nature of the laboratory procedures to be conducted in a facility (e.g. small- versus large-scale amplification, use and storage of the agent).</p> | <p>Moderate to severe</p> <ul style="list-style-type: none"> • Procedures such as antigen or vaccine production that generate large amounts of organism. • Aerosols generated by laboratory procedures (homogenisation, sonication, centrifugation). • Sample history: agents on primary isolation/low passage number are often more virulent than laboratory-adapted strains. | <p>GMT such as decontamination and disinfection, the use of effective infection control procedures including the use of proper primary containment systems to physically separate the process from the other work areas. Staff safety including agent/procedure-specific training and medical surveillance. The containment area(s) should be designed to contain spillage of the entire contents of the closed system. Inadvertent carriage from the area to be taken into consideration depending on the epidemiology of the disease and the impact on the animal disease situation in the country or region. Mandatory laboratory security policies and procedures: redundancy of control measures, access control, due diligence in authorising personnel, inventory of seed and working stocks, intrusion detection, emergency response plans</p> |
| | <p>Low:</p> <ul style="list-style-type: none"> • Vector or intermediate host required in the life-cycle of the agent does not naturally occur or survive in the country or region | <p>GMT such as decontamination and disinfection, effective infection control procedures including proper laboratory design, use of dedicated laboratory clothing, primary containment systems such as biosafety cabinets, and disinfection of laboratory wastes may be adequate. The risk of inadvertent carriage from the laboratory to be considered depending on the epidemiology of the disease and the impact on the animal disease situation in the country or region.</p> |
| <p>Use of animals in association with the biological agent or toxin.</p> | <p>A higher level of risk may arise when agents are inoculated into laboratory animals. The following factors should be considered in the risk assessment:</p> <ol style="list-style-type: none"> i) Host species versus inoculated species; ii) Strain, treatment and concentration of the inoculum; iii) Route of inoculation; iv) Animal housing; v) Types of sampling during the experiment. <p>Examples:</p> <ul style="list-style-type: none"> • Production of biological reagents (e.g. antibody) in animals • Animal-based diagnosis, pathogenicity determinations • Research | <p>Good animal handling and microbiological technique such as decontamination and disinfection, infection control procedures, protective clothing and proper equipment. Staff training and medical surveillance. The facility should be designed to minimise or prevent spread of the biological agent or toxin through contaminated air, laboratory materials, liquid or solid waste or animal carcasses. Pest control. The room is considered primary containment for large animals. For laboratory animals individual vented cages, isolators, or similar provide primary containment.</p> <p>Security considerations include prevention of intentional animal or agent release as a form of bioterror: perimeter fences, identification, intrusion alarms, redundancy of control measures.</p> |

Note: The control measures provided are not meant to be comprehensive, but are examples of available control measures. Comprehensive information on applicable biosafety and biosecurity measures is available in internationally recognised technical manuals such as the WHO Biosafety Manual (WHO, 2004), the Biosafety in Microbiological and Medical Laboratories (CDC, 2009) and related guides.