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Biosafety and biosecurity in veterinary laboratories

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Summary
With recent outbreaks of Middle East respiratory syndrome coronavirus (MERS-CoV), anthrax, Nipah and the highly pathogenic avian influenza virus, much emphasis has been placed on the rapid identification of infectious agents globally. As a result, laboratories are building capacity, conducting more advanced and sophisticated research, increasing their staff, and establishing reference collections of dangerous pathogens in an attempt to reduce the impact of infectious disease outbreaks and to characterise disease-causing agents. With this expansion, the global laboratory community has started to focus on laboratory biosafety and biosecurity in order to prevent the accidental and/or intentional release of these agents. Laboratory biosafety and biosecurity systems are used around the world to help to mitigate the risks posed by dangerous pathogens in the laboratory. Veterinary laboratories carry unique responsibilities with regard to workers and communities to handle disease-causing microorganisms safely and securely. Many microorganisms studied in veterinary laboratories not only infect animals, but also have the potential to infect humans. This paper will discuss the fundamentals of laboratory biosafety and biosecurity.

Keywords
Biorisk communication – Biorisk mitigation – Biosafety – Biosecurity – Laboratory biorisk management – Risk assessment.

Introduction

Infectious livestock diseases pose a significant risk to global animal health, and their control is essential to preserve international trade agreements pertaining to livestock and livestock products, to support economic growth and development, to promote and foster sustainable livelihoods and food security, and to prevent zoonoses in humans (1). Laboratory activities, including pathogen research, diagnostic tool development, pharmaceutical and vaccine development, and the identification and characterisation of aetiological agents, are critical to most successful control initiatives. While many of these activities clearly benefit animal health, the handling, isolation, storage, and disposal of infectious pathogens pose inherent safety and security risks to laboratories, their staff, the community, the environment and even the world. As a result, laboratory biosafety and biosecurity systems must be an integral part of any laboratory working with and handling dangerous microorganisms in order to prevent accidental and/or intentional release. The *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*) of the World Organisation for Animal Health (OIE) defines laboratory biosafety as 'the principles and practices for the prevention of unintentional release of or accidental exposure to biological agents and toxins' and laboratory biosecurity as 'the physical control of biological agents and toxins within laboratories, in order to prevent their loss, theft, misuse, unauthorised access or intentional unauthorised release' (2).

Laboratory accidents and the unintentional release of pathogens from veterinary laboratories can infect human and animal populations. The risk of laboratory-acquired infections was first described in 1951 following a comprehensive survey of 5,000 United States (US) laboratories documenting a presumed 1,300 laboratory-acquired infections with 39 deaths (3). Since then, numerous laboratory-acquired infections have been recorded. Two notable examples of such infections include an incident in Singapore where a microbiology student contracted the severe acute respiratory syndrome (SARS) virus after working in a contaminated laboratory biosafety cabinet, and another where work was suspended at a

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US laboratory when workers contracted brucellosis and were exposed to Q fever (4, 5).

Although animal health and research laboratories handle animal pathogens primarily, many of these pathogens are zoonotic. Consequently, these agents pose significant risks to laboratory staff and surrounding human and animal populations. Moreover, improperly inactivated laboratory waste containing pathogens, infected research animals, and/or contaminated laboratory staff and their possessions can contaminate the environment and infect surrounding communities and/or livestock. A notable example of this, which resulted in a catastrophic outcome, occurred in August and September 2007 in Surrey, the United Kingdom (UK), when laboratory strains of foot and mouth disease (FMD) virus leaked from a laboratory waste pipe, and were transmitted to local livestock through vehicles contaminated by the waste (6). The virus was detected in ten farms, and resulted in severe disruptions to the livestock sector costing more than £100 million to control (6). Given the potential consequences of accidental pathogen release, laboratory biosafety policies and practices are essential for any laboratory handling pathogens that pose a risk to human and animal health.

In addition to accidental release, deliberate dissemination of dangerous pathogens is an evolving threat. The rise in terrorist activities along with advancements in the life sciences increases the risk that pathogens could be used for malicious purposes (7). Using a biological agent to inflict harm is a complex multistep process that requires the acquisition of a pure and virulent pathogen, sufficient production, and effective dissemination (8). Experts suggest that terrorists are more likely to seek pathogens from bioscience laboratories due to their purity and established virulence, than from nature or naturally occurring outbreaks where the agent must be isolated and its virulence determined (8, 9, 10). Many types of research, diagnostic and pharmaceutical laboratories isolate, amplify and retain dangerous pathogens in order to conduct research, diagnose disease and establish efficacious therapies. Consequently, these pathogens are vulnerable to theft and potential misuse, and must be protected through the implementation of laboratory biosecurity programmes. Numerous accounts of the unauthorised acquisition of biological materials from legitimate bioscience facilities for use in bio-crimes have been documented (11). However, it was not until a laboratory strain of *Bacillus anthracis* was disseminated through the US postal system that strict guidelines to enhance laboratory biosecurity were established in several countries (8). Laboratory biosecurity systems are necessary to ensure that pathogens, information, and technologies are protected against theft and misuse.

Laboratory biorisk management systems

Biorisk management is a system of processes and procedures used to reduce the safety and security risks associated with the handling, storage and disposal of biological agents and toxins in laboratories (12). Laboratory biosafety and biosecurity are essential components of biorisk management that should be employed in all biological research laboratories based on the biorisk, or the probability that an adverse event, such as an accidental infection or intentional release, will occur, and the consequences of that event. Laboratory biosafety systems consist of engineering controls, standard work practices and personal protective equipment (PPE). Biosecurity systems consist of physical security, personnel security, information security, transportation security, and material control and accountability. While separate concepts, it is important to recognise that both are complementary and both share a common goal: to keep the laboratory, the community, and the environment safe and secure.

Chapter 1.1.4 of the OIE's *Terrestrial Manual*, 'Biosafety and biosecurity: standard for managing biological risk in the veterinary laboratory and animal facilities', describes the components of biorisk management as:

– biohazard identification
– biological risk assessment
– risk management
– risk communication
– verification with continual improvement (2).

Biohazard and asset identification

Before a laboratory's risks can be fully assessed and characterised, biohazards and assets must be identified. Hazard and asset identification answers the question: what can go wrong? More specific questions can be asked and include:

– What is the risk of infection?

– What is the risk to individuals (humans/animals) outside the laboratory?

– What is the risk of the theft of biological materials or equipment?

– What is the risk of selling or destroying biological materials, equipment, intellectual property, or personnel information for personal gain?

Animal-handling injuries, burns, punctures from sharps, exposure to hazardous chemicals and other non-biological risks from working with biological materials must be taken into account as well.

When identifying biosafety biorisks, it is important to identify the biological hazards that could cause harm. The biological characteristics of each agent are used to determine how hazardous the agent is, including its routes of infection, infectious dose, mortality/morbidity rates, stability in the environment, virulence, documented laboratory-acquired infections and host range, and the availability of preventative and therapeutic treatments. At-risk hosts are those vulnerable to infection that may be inside or outside the laboratory and may include humans, wildlife, livestock and other domestic animals.

When identifying biosecurity biorisks, it is important to identify all assets, including anything of value to the institution or an adversary such as biological material, equipment, intellectual property and possibly even laboratory animals. The identification of assets should consider the impact on the facility (financial, reputational or potential scientific impact) from the theft or destruction of the asset, and the potential impact on the environment or the facility of the misuse of the asset. These assets can be determined based upon their attractiveness to an adversary who may wish to pursue them. Thus, adversarial types, motive, means, opportunities and potential attacks should be considered.

Biological risk assessment

The backbone of laboratory biosafety and biosecurity is the biorisk assessment (13). Owing to the fact that each laboratory is unique, its risks will be unique. Thus, all risks should be considered and prioritised for each laboratory. A standardised and repeatable risk assessment process is necessary in order to identify changes over time, facilitate clear risk communication and ensure compliance with biorisk management best practices. Many biorisks may exist, including accidental or intentional exposure of staff, the community and/or the environment, and the risk of theft of biological materials, laboratory equipment or information. The questions posed to understand risk include:

– What can go wrong?

– How likely is it to happen and how likely would we be to anticipate it?

– What are the consequences? (14)

A biosafety and biosecurity risk assessment should be performed to ensure that awareness is created of all of the risks faced by a laboratory or biomedical facility and of the mitigation of these risks.

Collecting data for a laboratory biosafety and biosecurity risk assessment should be a shared responsibility between principal investigators, scientists, researchers (or a risk assessment team) and biorisk management advisors. After the information necessary to conduct a risk assessment has been gathered, an overall characterisation of biorisk is conducted. In terms of biosafety, the likelihood and consequences of an infection or contamination event are determined. For biosecurity, the likelihood and consequences of theft or acquisition are the focus. Considering the consequences of adverse events is critical to risk characterisation. The health effects, potential to spread and/or economic effects of a release (intentional or accidental) must be considered. This is often location-specific; for example, the release of an agent into a region where the disease is enzootic can have less severe consequences than if it were released into an area from which the disease had been eradicated. Depending on the situation, the facility should decide if the work with biological materials can proceed with safeguards or if it should be refused.

Risk management

Risk management can be described in terms of mitigating identified laboratory biorisks, and refers to actions and control measures put into place to reduce or eliminate the risks associated with biological agents and toxins based on the laboratory risk assessment. The assessed and accepted risks determine the actions and control measures that will be most effective in reducing and eliminating those particular risks. Monitoring the performance of the chosen mitigation measures is also required to ensure that the mitigation controls are reducing risks to an acceptable level.

Biosafety risk mitigation systems aim to protect humans, animals or the environment from an accidental exposure or release from a laboratory. Biosecurity risk mitigation systems seek to protect assets from intentional theft, diversion or release by malicious individuals inside or outside the laboratory. The safety and security control approaches are often complementary and should be used in combination so as to accomplish appropriate risk reduction, but there are advantages and disadvantages to each. Mitigation control options for laboratory biosafety and biosecurity are categorised as:

– elimination or substitution
– engineering controls
– administrative controls
– operational controls
– PPE (15).

Elimination or substitution

Mitigation of both laboratory biosafety and biosecurity risks can be done by eliminating the biological agent or toxin altogether, or by substituting it with a less hazardous pathogen. Elimination removes all risk of accidental exposure and theft, and provides the highest degree of risk reduction. The substitution of an agent with a less virulent pathogen with similar biological characteristics allows the researcher to carry out the necessary research at inherently lower safety and security risks. Both of these approaches are favoured control strategies to reduce risk, and they are also likely to be less expensive and require less maintenance (16).

If elimination or substitution of the risk is not possible, additional control strategies such as administrative, operational, engineering and PPE controls (described below) are used to minimise the safety concerns associated with accidental release and the security concerns associated with intentional release.

Engineering controls

Engineering controls are physical changes to workstations; the use of specialised equipment, materials or production facilities; or any other relevant aspect of the work environment that reduces the risk of accidental or intentional release. Primary containment refers to engineering controls to increase the safety of research personnel and reduce the risk of the intentional removal of biological material from the laboratory. Secondary containment refers to engineering controls that reduce the risk of release to the environment or surrounding community outside the facility.

Engineering controls are an effective, yet often misused, strategy to reduce biorisks. Laboratories are often designed around engineering controls, which can provide a false sense of safety and security. Cost, available resources, existing infrastructure and the availability of trained personnel must be considered when choosing these controls. Engineering controls alone are not sufficient to ensure safety and security in a laboratory; they are only one component of a comprehensive biorisk management programme, and should be selected in coordination with other desired controls. Engineering controls generally protect staff as well as the environment and community, but require resources, applicability and maintenance to reduce risks effectively.

Examples of engineered biosafety controls include

– biosafety cabinets

– chemical fume cupboards

– changes to the physical features of the facility that allow for better ventilation and airflow

– barrier walls and shields

– separation of incompatible activities

– alternative diagnostic tools

– equipment maintenance, calibration and certification.

Likewise, engineered biosecurity controls to reduce the risks of theft or unauthorised access to biological material or other assets include:

– access controls (e.g. access restrictions such as keys, locks, and badge and personal identification number readers)

– alarms and/or other detectors

– perimeter fences and gates.

Administrative controls

Administrative controls are policies, procedures, standards and guidelines used to control biorisks. This may include health monitoring programmes, inventory systems and training programmes.

Worker health programmes can support biosafety by protecting workers through prophylactic vaccinations and/or healthcare monitoring to identify rapidly personnel who may be infected, ill or susceptible to future infections. Hiring qualified staff, implementing emergency response and contingency plans, posting signage and preparing documentation in the form of biosafety plans or manuals, and standard operating procedures (SOPs) are other forms of biosafety administrative controls.

Biological sample inventory and life-cycle management are vital components of administrative mitigation controls, which benefit both biosafety and biosecurity. Other examples include the development and maintenance of current biological agents and toxin inventory, and inventory management requirements including:

– access, storage, transfer (shipping, receiving and sample transport), destruction and audit (also referred to as material control and accountability)

– waste management policies

– documentation regarding security policies, including facility security, visitor access, personnel management, and access to biological agents and toxins (also referred to as personnel security)

– information security.

Training is another type of administrative control that is important for mitigating safety and security risks. A biorisk management training programme is only effective at reducing risk when a training needs assessment is conducted and a training programme is executed based on well-established training models, such as the ADDIE

model (Analysis, Design, Development, Implementation and Evaluation model) (17). The entire workforce, including management, laboratory technicians, custodial staff, maintenance personnel and security forces, must be included in the training programme in order to ensure that all employees are cognisant of the laboratory's policies and the biorisk management system, commensurate with their individual roles and responsibilities.

Operational controls

Operational controls are mitigation controls that employ SOPs and internationally accepted practices to improve biorisk management. They are designed to guide personnel with precise instructions on how to carry out tasks consistently and efficiently, and should be routinely observed, evaluated and validated by staff to maximise comprehension. The written documentation is an administrative control, but the process of performing procedures as specified must be continuously evaluated. The procedures require evaluation for document relevance, necessary training for those carrying them out, and evaluation of the effectiveness of safety and security measures.

Standard operating procedures can be developed for a variety of practices and procedures for both laboratory biosafety and biosecurity. Depending on the work performed in a given laboratory, biosafety SOPs may target pathogen-handling, sample analysis, waste disinfection and decontamination, and safety emergency incident response events, among others. Examples of biosecurity SOP objectives may include:

– sample transport
– pathogen storage
– the operation of physical security systems
– emergency incident response events
– identification badge usage
– visitor control
– personnel management procedures
– security force procedures
– security incident response plans.

Personal protective equipment

When used correctly, PPE is a biosafety mitigation control that provides protection to individual workers from the most hazardous pathogens and chemicals. PPE selection is based on the work conducted and the pathogens handled, thus, it is dependent upon the risk assessment. A variety of PPE is commercially available to prevent serious safety injuries, including laboratory coats, safety glasses, face shields, N95 and N100 respirators, and gloves. These are devices worn by workers to protect them against chemicals, toxins and pathogenic hazards in the laboratory. PPE is considered the least effective control strategy, as it protects only the person wearing it.

The effectiveness of PPE to reduce risk also relies on administrative and operational controls regarding its purchase, storage, use, 'donning' (putting on) and 'doffing' (removing), and waste disposal procedures. The performance of PPE use and appropriate procedures must also be monitored to ensure effective risk management.

Risk communication

Biorisk communication is the interactive transmission and exchange of information and opinions throughout the risk analysis process on risk, risk-related factors, and risk perceptions among risk managers, risk communicators, the general public and other impacted parties (2). Because laboratories handling animal and zoonotic pathogens are an essential piece of a country's veterinary infrastructure, it is important that a laboratory's benefits, risks and biological risk mitigation plans are transparent, and clearly communicated to all relevant stakeholders (14). Laboratory staff, the surrounding community, livestock owners, policy-makers, and government authorities are all pertinent stakeholders, and the information shared with each should be tailored to its specific audience in order to address its individual concerns and level of required technical knowledge. This will help to prevent misinterpretations and miscommunications.

Effective biorisk communication ensures transparency to minimise the fear and apprehension that might be expressed over possible exposures, and conveys laboratory risks accurately and calmly. Messages, language and literature should be tailored to provide clear and understandable information concerning the work being conducted.

Verification with continual improvement

Biological risks in the laboratory are dependent on the work performed, and must therefore be reassessed each time a practice or procedure changes or is implemented. The laboratory facility, management practices and procedures should also be regularly evaluated so as to ensure that changes have not altered previously established risks. Effective performance measurements can call attention to practices that are no longer adequate or that are failing over time.

Burnett and Olinger, in *Laboratory Biorisk Management* (18), propose a more thorough measure of performance to replace conventional audits and surveys that would establish performance indicators during system development, which includes:

i) establishing priorities where risk is greatest

ii) defining the indicators and metrics for the success of a given outcome

iii) defining the indicators and metrics for the success of a given activity

iv) collecting data and report results

v) responding to findings

vi) improving performance indicators.

This system provides the end user with a more standardised method of evaluation that includes laboratory staff in the evaluation process. Continuous performance evaluation provides the staff and stakeholders with confidence in the system, and also helps to lend sustainability to the practices and procedures (2).

Responsible capacity-building

Strengthening capacity in a laboratory is essential in order to detect, assess, respond and monitor disease events within a country successfully. Developing such capacity requires both commitment and resources within a laboratory network. Generally speaking, laboratory capacity is well developed in industrialised countries and poorly so in most low- and limited-resource countries, many of which are home to dangerous endemic human and animal pathogens, devastating infectious disease outbreaks, and organisations that may want access to dangerous pathogens, equipment and/or information (19). Consequently, various international, governmental and non-governmental organisations attempt to boost laboratory capacity in many of these countries through the purchase of laboratory equipment and/or the technical training of laboratory personnel in the hopes of improving national biosurveillance and reducing the threat of biological acquisition.

Yet, responsible and sustainable laboratory capacity-building requires more than supplying a laboratory with sophisticated equipment and advanced personnel training. Any laboratory capacity-building effort with the aim of reducing the spread of infectious diseases is obligated to include an awareness of, and require a long-term commitment to, recognising and mitigating a laboratory's biosafety and biosecurity risks.

It is imperative that efforts to improve laboratory capacity do not inadvertently, or unnecessarily, increase the risk of biological acquisition and/or the risk of accidental exposure. These risks are inherently present when obtaining, isolating, manipulating and storing dangerous, and most importantly, unnecessary, animal or zoonotic material at a laboratory. Capacities that affect both biosafety and biosecurity would include the acquisition of laboratory equipment and/or reagents that enhance the capacity to culture, propagate and/or store dangerous pathogens. Specific biosecurity risks may include equipment that could be considered of dual use, including biosafety cabinets and PPE. Once acquired by nefarious individuals, some laboratory equipment and PPE may allow for the proliferation of practices that were once previously too dangerous to practise. It is also important to be aware that even educational training of personnel that increases a laboratory's technical capacity could be misused to increase and disseminate dangerous biological pathogens. Specific capacities that affect biosafety would include the acquisition of any piece of equipment or the application of any procedure that may increase the potential for release, exposure and infection. This would include, for example, research procedures that involve the increased handling of dangerous animal and zoonotic agents and/or equipment that creates aerosols or the potential for spilling.

Instead, efforts should focus on implementing a responsible laboratory capacity that improves a laboratory's ability to detect disease, but at the same time complements that laboratory's biosafety and biosecurity profile. This can be accomplished by reducing the amount of unnecessary biological material and dual-use equipment stored and handled at the facility, as well as by implementing protocols and procedures that would reduce the laboratory's reliance on equipment or material. For any essential biological material or equipment that must be retained for mission-critical laboratory purposes, a complete and robust biosafety and biosecurity risk assessment should be executed and any identified risks mitigated appropriately. Any personnel training that divulges technical capabilities that may pose a proliferation risk should be evaluated critically as to its absolute necessity and all technical training should include an awareness of the dual-use issues associated with biological laboratory work. Lastly, capacities should also contribute towards providing additional risk mitigation by including provisions for PPE against exposure and infection for laboratory staff during routine research.

Conclusion: challenges and sustainability

The design and implementation of a large-scale biorisk management system may be overwhelming unless a standardised risk-based approach is used. Identifying and

assessing hazards helps laboratory managers to prioritise resources in order to mitigate the greatest risks. In most cases, risks can be controlled using elimination and substitution, targeted engineering controls, administrative controls, operational controls and PPE. Using a standard approach to biorisk management that includes laboratory staff and measures laboratory performance helps to build a sustainable and effective system. Moreover, it creates a culture of biorisk management in the laboratory.

Few published data are available on the sustainability or effectiveness of laboratory biosafety and biosecurity systems globally. However, sustaining biorisk management systems is complex and dependent on a mixture of factors, including inherent risks, available resources, regulatory requirements, effective laboratory policies, management commitment and determination, and laboratory culture (20). In most laboratories, laboratory biosafety is fundamentally appreciated and practised. Most laboratory personnel and researchers intrinsically appreciate the need to protect themselves and their communities from accidental exposures. However, the concept of laboratory biosecurity is a more recent one, and consequently, the value of such programmes may be overlooked.

In conclusion, this paper emphasises the importance of cultivating a culture of biorisk management that encompasses both safety and security in a laboratory's daily routine. The collection, transport, isolation and storage of such agents pose inherent risks that must be managed in order to support the efficient and timely control of a dangerous outbreak of infectious diseases as well as improve the quality of work performed in the laboratory. Recent outbreaks of dangerous human and animal disease, and the lessons learned from these outbreaks, underscore the importance of robust biorisk management systems and their sustainability.

La biosécurité et la biosûreté dans les laboratoires vétérinaires

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Résumé

Suite aux nombreux foyers récents dus à divers agents pathogènes (coronavirus responsable du syndrome respiratoire du Moyen-Orient [MERS-CoV], agent de la fièvre charbonneuse, virus Nipah, virus de l'influenza aviaire hautement pathogène), la nécessité d'identifier rapidement les agents pathogènes en n'importe quel endroit de la planète est désormais au centre des préoccupations. Par conséquent, les efforts des laboratoires sont axés sur le renforcement des capacités, la conduite de travaux de recherche de pointe de plus en plus spécialisés, l'accroissement des effectifs et l'élaboration de référentiels d'agents pathogènes dangereux dans le but de réduire l'impact des foyers de maladies infectieuses et de caractériser les agents responsables de ces maladies. Dans ce contexte d'activité accrue, le réseau international des laboratoires a commencé à accorder une grande importance aux questions de biosûreté et de biosécurité afin de se prémunir contre le risque de libération accidentelle et/ou délibérée de ces agents pathogènes. Les systèmes de biosécurité et de biosûreté sont appliqués dans le monde entier pour contribuer à l'atténuation des risques liés aux agents pathogènes dangereux détenus par les laboratoires. Les laboratoires vétérinaires ont à l'égard de leur personnel et de la société tout entière la responsabilité majeure de garantir la sécurité et la sûreté de la manipulation des microorganismes pathogènes. En plus d'infecter les animaux, nombre des microorganismes analysés dans les laboratoires vétérinaires ont également un potentiel zoonotique. Les auteurs examinent les aspects essentiels de la biosécurité et de la biosûreté au laboratoire.

Mots-clés

Appréciation du risque – Atténuation des risques biologiques – Biosécurité – Biosûreté – Communication sur les risques biologiques – Gestion des risques biologiques au laboratoire.

Seguridad y protección biológicas en los laboratorios veterinarios

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Resumen

Los recientes brotes de coronavirus del síndrome respiratorio de Oriente Medio (MERS-CoV), carbunco bacteridiano, virus de Nipah y virus de la influenza aviar altamente patógena han llevado a hacer especial hincapié en la rápida identificación de agentes infecciosos a escala mundial. Obrando en consecuencia, los laboratorios están dotándose de medios de acción, llevando a cabo investigaciones más avanzadas y sofisticadas, reforzando su plantilla y creando colecciones de referencia de patógenos peligrosos con la voluntad de reducir los efectos de los brotes infecciosos y caracterizar a los agentes patógenos. Al mismo tiempo, en todo el mundo los profesionales del ramo han empezado a prestar atención a la seguridad y la protección biológicas en el laboratorio, con el fin de prevenir toda liberación accidental y/o deliberada de los mencionados agentes. Los laboratorios del mundo entero emplean sistemas de seguridad y protección biológicas como elemento auxiliar para reducir los riesgos derivados de la presencia de patógenos peligrosos en sus instalaciones. Los laboratorios veterinarios tienen una especial responsabilidad para con los trabajadores y las poblaciones por lo que respecta a la manipulación de microorganismos patógenos en las debidas condiciones de seguridad y protección. Muchos de los microorganismos estudiados en los laboratorios veterinarios infectan no solo a los animales, sino también, en potencia, al ser humano. Los autores examinan los aspectos fundamentales de la seguridad y la protección biológicas en laboratorio.

Palabras clave

Comunicación del riesgo biológico – Determinación del riesgo – Gestión del riesgo biológico en laboratorio – Mitigación del riesgo biológico – Protección biológica – Seguridad biológica.

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