Uploaded to the VFC Website

May 2015

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

If Veterans don't help Veterans, who will?

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members & subscribers.

WHO/CDS/EPR/2006.6

Biorisk management

Laboratory biosecurity guidance

September 2006

EPIDEMIC AND PANDEMIC
ALERT AND RESPONSE

World Health Organization

Biorisk management

Laboratory biosecurity guidance

September 2006

World Health Organization

© World Health Organization 2006

All rights reserved.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Table of Contents

Abbreviations

BSL3 Containment laboratory – Biosafety Level 3

BSL4 Maximum containment laboratory – Biosafety Level 4

FAO Food and Agriculture Organization of the United Nations

GMO Genetically modified organism

LBM3 Laboratory biosafety manual, third edition, 2004

LBG Biorisk management: laboratory biosecurity guidance, first edition, 2006

OIE World Organisation for Animal Health

VBM Valuable biological materials

WHO World Health Organization

Definitions

The following terms are defined in the context in which they are used in this document.

Accountability
Accountability ensures that valuable biological materials (VBM, see definition below) are controlled and traced as intended, by formally associating the specified materials with the individuals who provide oversight and are held responsible for them.

Bioethics
The study of the ethical and moral implications of biological discoveries, biomedical advances, and their applications as in the fields of genetic engineering and drug research (adopted from *1*). In this document, bioethics is one of the three components that contribute to a successful biorisk management culture.

Biological laboratory
A facility within which microorganisms, their components or their derivatives are collected handled and/or stored. Biological laboratories include clinical laboratories, diagnostic facilities, regional and/national reference centres, public health laboratories, research centres (academic, pharmaceutical, environmental, etc.) and production facilities (manufacturers of vaccines, pharmaceuticals, large scale GMOs, etc) for human, veterinary and agricultural purposes.

Biorisk
The probability or chance that a particular adverse event (in the context of this document: accidental infection or unauthorized access, loss, theft, misuse, diversion or intentional release), possibly leading to harm, will occur.

Biorisk assessment
The process to identify acceptable and unacceptable risks (embracing biosafety risks (risks of accidental infection) and laboratory biosecurity risks (risks of unauthorized access, loss, theft, misuse, diversion or intentional release)) and their potential consequences.

Biorisk management
The analysis of ways and development of strategies to minimize the likelihood of the occurrence of biorisks. The management of biorisk places responsibility on the facility and its manager (director) to demonstrate that appropriate and valid biorisk reduction (minimization) procedures have been established and are implemented. A biorisk management committee should be established to assist the facility director in identifying, developing and reaching biorisk management goals.

Biosafety
Laboratory biosafety describes the containment principles, technologies and practices that are implemented to prevent the unintentional exposure to pathogens and toxins, or their accidental release (*2*).

Code of conduct, code of ethics, code of practice
Non-legislated guidelines which one or more organizations and individuals voluntarily agree to abide by, that set out the standard of conduct or behavior with respect to a particular activity (adopted from *1*).

Control
Control is the combination of engineered and procedural measures that ensure valuable biological material (VBM, see definition below) are used only as intended.

Dual-use
Initially used to refer to the aspects of certain materials, information and technologies that are useful in both military and civilian spheres. The expression is increasingly being used to refer not only to military and civilian purposes, but also to harmful misuse and peaceful activities (adopted from *1*).

Genetically modified organisms (GMO)
Organisms whose genetic material has been altered using techniques generally known as "recombinant DNA technology". Recombinant DNA technology is the ability to combine DNA molecules from different sources into one molecule in a test tube. GMOs are often not reproducible in nature, and the term generally does not cover organisms whose genetic composition has been altered by conventional cross-breeding or by "mutagenesis" breeding, as these methods predate the discovery (1973) of recombinant DNA techniques.

Hazard
A danger or source of danger; the potential to cause harm.

Laboratory biosecurity
Laboratory biosecurity describes the protection, control and accountability for valuable biological materials (VBM, see definition below) within laboratories, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release.

Misuse
The misuse of valuable biological materials (VBM, see definition below) describes their inappropriate or illegitimate use, despite existing and subscribed agreements, treaties and conventions (*3*).

Threat
The likelihood for an adverse event to occur, as an expression of intention to inflict evil, injury, disruption or damage.

Transfer of VBM
Legal and/or administrative policies and procedures relating to the oversight and approval process for the transfer of custody and/or ownership of valuable biological materials (VBM, see definition below) between countries, entities (organizations, institutions, facilities, etc.) or individuals.

Transport of VBM
Procedures and practices to correctly categorize, package, document and safely and securely transport valuable biological materials (VBM, see definition below) from one place to another, following applicable national and/or international regulations.

Valuable biological materials (VBM)
Biological materials that require (according to their owners, users, custodians, caretakers or regulators) administrative oversight, control, accountability, and specific protective and monitoring measures in laboratories to protect their economic and historical (archival) value, and/or the population from their potential to cause harm. VBM may include pathogens and toxins, as well as non-pathogenic organisms, vaccine strains, foods, genetically modified organisms (GMOs), cell components, genetic elements, and extraterrestrial samples.

Preface

The economic consequences and scientific concern resulting from the laboratory-acquired SARS-CoV infections of 2003-2004 in Singapore, Taipei and Beijing not only raised biosafety awareness in the affected facilities, but most importantly promoted review by the concerned scientific community and national regulatory bodies, demonstrating high political commitment to biosafety practices in laboratories. The incidents triggered the improvement of national biosafety policies. Other countries affected, whether directly or indirectly, also expressed wide-ranging concern. As a result, WHO has recently witnessed a worldwide increase in the demand for biosafety guidance and support that culminated in 2005 with the adoption by the World Health Assembly of resolution WHA58.29 on *Enhancement of laboratory biosafety* (*4*).

The *Laboratory biosafety manual* (LBM3), published in 2004 in its third edition (*2*), has already provided guidance to laboratory workers on how to perform laboratory work safely, to laboratory managers on how to set up a managerial approach to biosafety and to regulatory authorities, to help them consider necessary aspects for the development of adequate national biosafety regulations. A top-down approach associated with bottom-up support for biosafety regulations has been very successful in advancing the biosafety agenda.

The present document aims to expand the laboratory biosecurity concepts introduced in LBM3, and to strike a balance between the long-known biosafety procedures and practices described in LBM3 and the more recently introduced and broader biosecurity concepts. It further introduces the overarching "biorisk management" approach that has resulted from careful thinking, comprehensive study of prevailing practices and recommendations, review of international norms and standards, and relevant ethical considerations Shortcomings currently observed in a number of settings are discussed, and practical solutions are proposed.

The document is intended for the use of relevant national regulatory authorities, laboratory directors (laboratory managers) and laboratory workers, all of whom play key roles in the field of biosciences and in public health in general.

1. Introduction

Background

Disease diagnosis, human or animal sample analysis, epidemiological studies, scientific research, and pharmaceutical developments: all of these activities are carried out in biological laboratories in the private or public sectors. Biological materials are handled worldwide in laboratories for numerous genuine, justifiable and legitimate purposes, where small and large volumes of live microorganisms are replicated, where cellular components are extracted and many other manipulations undertaken for purposes ranging from educational, scientific, medicinal and health-related to mass commercial and/or industrial production. Among them, an unknown number of the facilities, large and small, work with dangerous pathogens or their products every day.

The general public expects laboratory personnel to act responsibly and not to expose the community to biorisks, to follow safe working practices (biosafety) associated with practices that will help keep their work and materials safe and secure (biosecurity), and to follow an ethical code of conduct (bioethics). Often suspicious of work taking place in laboratories, the uninformed public may even feel threatened by the presence of a biological laboratory in their neighborhood. It is the technical and moral duty of laboratory managers and laboratory workers, with the support of national authorities, to reassure the general public, to persuade them that the activities being conducted are beneficial and necessary, and to prove that the biorisks inherent to laboratory work are controlled with appropriate safeguards to meet their expectations.

However, despite advances in technology, the availability of more and more sophisticated instruments for laboratory use, increasingly effective techniques and the availability of personal protective equipment, human error remains one of the most important factors at the origin of accidents. Poor concentration, denial of responsibilities, inappropriate accountability, incomplete record-keeping, suboptimal facility infrastructure, refusal to acknowledge ethical considerations, lack of (or lack of respect for) codes of conduct, etc. may be at the origin of laboratory-acquired infections, loss of material and inappropriate manipulations, or even possibly intentional misbehaviour.

Pathogens and toxins have been used, even in the recent past, to threaten and harm people, to disrupt society, economies and the political status quo (*5*). This has happened in spite of applicable international agreements banning the use of biological agents for malicious use. As those who carry out such acts show disregard for ethical values (*6*), do not respect the right of people to a safe and peaceful life, or do not recognize global treaties and conventions, several regulatory approaches to limit unauthorized access to biological agents and toxins available in biological laboratories are now being carefully considered and implemented worldwide.

Three examples illustrate the need to respond to the international community and articulate biosecurity in the laboratory:

1. Smallpox has been eradicated some 26 years ago. However, its causative agent, variola virus, remains stored in two WHO Collaborating Centres under maximum containment. The accidental or deliberate reintroduction of variola virus into the environment threatens not only public health, but also the economy and political stability of the whole world. For this reason, the known remaining variola virus stocks are subject to WHO scrutiny for the research they are subject to (*7*), and each site is regularly assessed by WHO for its biosafety and laboratory biosecurity (*8*). Despite these existing international arrangements, this guidance document offers an opportunity for further improvement of their working and storage conditions.

2. As the final stages of the poliomyelitis eradication campaign approach, steady progress is being made towards the safe-keeping of facilities containing poliovirus samples and stocks, which will then be advised to decide whether to keep these polioviruses and upgrade their biosafety containment and biosecurity levels and tighten their codes of conduct, transfer their poliovirus samples to a better-equipped reference laboratory, or destroy the remaining stocks. Experience gained and lessons learnt from the containment of variola viruses post eradication offer an invaluable opportunity to plan for the polio post eradication phase and for the development of most appropriate biorisk management plans and goals.

3. Laboratory biosecurity provisions may not have impeded the release of the anthrax letters in the USA in 2001 (*5*). In hindsight however, laboratory biosecurity provisions to write records on research and activity, access shared documentation, consult approved research projects and available results data, may have helped discharge alleged facilities and perpetrators from the list of possible suspects.

Historical awareness of the dual-use (*9*) of agents, equipment and technology, is also considered in the development of laboratory biosecurity guiding principles.

Current situation

Facilities containing biological agents may represent tempting procurement opportunities, thus advocacy for security-related scrutiny of biological facilities, their personnel and their visitors is increasing worldwide. In recent years, several countries have developed and implemented laboratory biosecurity legislation to regulate possession, use and access to biological materials to permit their appropriate use.

Despite the advances of some countries, in many other countries and for many laboratories, guidance or specific requirements for the appropriate handling and storage of valuable biological materials (VBM, described below) do not yet exist. This raises the following questions: How are these agents generally kept in such countries? Who has access to them? What kind of research is allowed and conducted with them? Who oversees this research? Who has the ultimate responsibility for these agents? Who should have access to information related to these agents, including research

results and storage details? Should research results be published? Is there a scrutiny for the publication of research data?

Many open questions still remain in the context of laboratory biosecurity, and much still needs to be done to reassure the public, scientists, laboratory managers, regulators, national authorities and the international community that the appropriate measures to prevent, manage, control and minimize the biorisks associated with possessing and handling infectious agents are in place. The biorisk management approach described in this document, encompassing biosafety and laboratory biosecurity, represents a step towards the clarification of these questions.

Globally, one common trend can be identified: rather than providing a prescriptive approach to addressing biosafety and related issues, and requesting compliance with a set of strict rules, the move to a goal-setting approach describing performance expectations for facilities, and placing the responsibility on single facilities to demonstrate that appropriate and valid biorisk minimization measures have been established, is proving very successful. Leaving the choice of procedures, control measures and verification systems to facility managers to ensure that set goals are reached requires the involvement of dedicated managers and of leaders who express appreciation for specific measures, and are instrumental in encouraging and supporting the development of a global biorisk management culture. Indeed it is such a biorisk management culture that the international bioresearch community should strive for.

International biorisk management

While an understanding of the need to safeguard VBM is becoming more widespread, universally agreed-upon laboratory biosecurity principles and practices are not. The resulting inconsistencies represent the complexity of the issue and a challenge for the international community to identify what should be addressed and how to respond to real needs. In the framework of public health, the challenge for the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the World Animal Health Organisation (OIE) is to provide Member States with balanced, appropriate and sustainable recommendations that address the biosecurity of biological materials in laboratory environments, expanding the strict mandates of these organizations in the fields of human and animal public health to the area of security, generally associated with entities that have law-enforcement mandates.

International organizations and agreements use the word biosecurity in a variety of contexts and for different purposes, in response to recommendations to protect different assets. FAO and OIE refer to biosecurity in the context of biological and environmental risks associated with food and agriculture, including forestry and fisheries, a sector that covers food safety, and the life and health of plants and animals. The risks include everything from the introduction and release of GMOs and their products, the introduction and spread of invasive alien species, alien genotypes and plant pests, animal pests and diseases and zoonoses, to the erosion of biodiversity, the spread of transboundary cattle diseases, or the preservation of food supplies after production.

The purpose of this document is to define the scope and applicability of "laboratory biosecurity" recommendations, narrowing them strictly to human, veterinary and agricultural laboratory environments. The operational premise for supporting national laboratory biosecurity plans and regulations generally focuses on dangerous pathogens and toxins. In this document, the scope of laboratory biosecurity is broadened by addressing the safekeeping of all *valuable biological materials* (VBM), including not only pathogens and toxins, but also scientifically, historically and economically important biological materials such as collections and reference strains, pathogens and toxins, vaccines and other pharmaceutical products, food products, GMOs, non-pathogenic microorganisms, extraterrestrial samples, cellular components and genetic elements. This is done in order to raise awareness of the need to secure collections of VBM for many reasons, including: for the sake of biology, to preserve biological diversity and endangered species, to perform microbiological studies and better understand the living world and the science behind it; to safeguard resources from which new drugs, vaccines and life-saving materials may be developed, for historical reasons, and to advance the state of knowledge.

Scope of this document

This document introduces a new concept and approach to minimize or prevent the occurrence and consequences of human error within the laboratory environment: the biorisk management approach, composed of biosafety, laboratory biosecurity and ethical responsibility.

Biosafety and its internationally acknowledged advantages have already been extensively described in LBM3. Laboratory biosecurity and its as yet poorly appreciated advantages and responsibility in coordinating personnel and scientific activities (research), and code of ethics are discussed here.

Within a comprehensive biorisk management approach, this document aims to define and guide the reader in the field of laboratory biosecurity. It is addressed to laboratories wishing to handle and store VBM, and discusses the legal framework within countries holding and supporting such laboratories. Setting the goal of managing biorisks should drive national authorities, laboratory managers and ultimately laboratory workers to take responsibility in developing the necessary safeguards. This in turn should demonstrate that biorisks in all their potential forms are appropriately addressed, managed and minimized.

Rationale

While Member States are expected to address laboratory biosecurity issues in the context of their regional, national and local situations and needs, this document provides guidance to help frame the concepts. A comparative description of biosafety and laboratory biosecurity is provided below for clarification.

Member States are encouraged to introduce these concepts within their local contexts and to develop national frameworks for the security of biological materials they consider valuable, in recognition of the ever-increasing importance of global regulatory harmonization (*10*). In the absence of national regulatory guidance, laboratory managers are encouraged to consider adopting a biorisk management approach adapted to their particular situation and developing guiding principles to be implemented in response to the specific needs of their facilities.

2. Laboratory biosecurity as a complement to laboratory biosafety

Laboratory biosafety and biosecurity mitigate different risks, but they share a common goal: keeping VBM safely and securely inside the areas where they are used and stored.

Laboratory biosafety (*2*) is the expression used to describe the containment principles, technologies and practices that are implemented to prevent unintentional exposure to pathogens and toxins, or their accidental release.

A comprehensive biosafety culture translates into the understanding and routine application of a set of safe practices, procedures, actions and habits that protect the people working with biological materials.

Laboratory biosecurity may be addressed through the coordination of administrative, regulatory and physical security procedures and practices implemented in a working environment that utilizes good biosafety practices, and where responsibilities and accountabilities are clearly defined. Biosafety and laboratory biosecurity are complementary. In fact, the implementation of specific biosafety activities already covers some biosecurity aspects. The systematic use of appropriate biosafety principles and practices reduces the risk of accidental exposure and paves the way for reducing the risks of VBM loss, theft or misuse caused by poor management or poor accountability and protection. Laboratory biosecurity should be built upon a firm foundation of good laboratory biosafety.

Through microbiological risk assessments performed as an integral part of an institution's biosafety programme, information is gathered regarding the type of organisms available at a given facility, their physical location, the personnel who require access to them, and the identification of those responsible for them. A laboratory biosecurity risk assessment should further help establish whether this biological material is valuable and warrants security provisions for its protection that may be insufficiently covered through recommended biosafety practices. This approach underlines the need to recognize and address the ongoing responsibility of countries and institutions to ensure the expectation for a safe and secure laboratory environment.

A specific laboratory biosecurity programme, managing the identified biorisks, should be prepared and designed for each facility according to its specific requirements, to the type of laboratory work conducted, and to local and geographical conditions. Laboratory biosecurity activities should be representative of the institution’s various needs and should include input from scientific directors, principal investigators, biosafety officers, laboratory scientific staff, maintenance staff, administrators, information technology staff, law-enforcement agencies and security staff, if appropriate. A sound code of practice should be included for personnel practice.

Laboratory biosecurity measures should be based on a comprehensive programme of accountability for VBM that includes:

1. regularly updated inventories with storage locations,
2. identification and selection of personnel with access,
3. plans of use of VBM,
4. clearance and approval processes,
5. documentation of internal and external transfers within and between facilities, and of any
6. inactivation and/or disposal of the material.

Likewise, institutional laboratory biosecurity protocols should include how to handle breaches or near-breaches in laboratory biosecurity including:

1. incident notification,
2. reporting protocols,
3. investigation reports,
4. recommendations and remedies, and
5. oversight and guidance through the Biosafety Committee.

The protocols should also include how to handle discrepancies in inventory results, and describe the specific training to be offered, and the training that personnel should be required to follow. The involvement, roles and responsibilities of public health and security authorities in the event of a security breach should also be clearly defined. Documenting procedures to manage behaviour and the interaction of workers with the facility and its equipment should also be considered.

These issues should be addressed according to a goal-setting approach to make sure the objective of minimizing biorisks is reached, rather than following a prescriptive approach to demonstrate compliance to a given set of rules. A goal-setting approach furthermore enables facilities to be creative, imaginative and innovative, allowing for responding to unexpected events, and for new findings and considerations to be easily incorporated into existing management systems. Goal-setting principles-based approaches enable staff to deal with the unpredicted and unfamiliar in the most prudent and safe manner until more expert opinion can be obtained.

2.1 Commonalities and conflicts: laboratory biosafety vs laboratory biosecurity

Commonalities

Good laboratory biosafety practices reinforce and strengthen laboratory biosecurity systems. Appropriate levels of biosafety may be achieved through carefully designed and implemented work practices, even in modestly-equipped facilities. The biosafety recommendations outlined in LBM3 provide clear levels of protection for VBM. For example self-closing doors, restricted access, physical separation from traffic areas, break-resistant windows and an emergency response plan may all be common to both biosafety and laboratory biosecurity.

LBM3 also advocates a "reliable and adequate electricity supply and emergency lighting" as well as a "stand-by generator". While this helps to ensure the function of critical biosafety equipment (ventilation systems, biological safety cabinets, autoclaves, etc.), it also supports components of physical security systems that may depend on electrical supply.

According to LBM3, the review of research protocols falls under the responsibilities of the biosafety officer and the biosafety committee, by delegation of the director of the facility. This includes risk assessments in consultation with local authorities, national regulatory bodies and the community for contentious or sensitive protocols under discussion. Adding the review of laboratory biosecurity to the existing biosafety mandate for biosafety committees represents a major change and an additional responsibility (*11*). The best advice to these committees is that they should follow transparent processes involving open discussions, and examine moral and ethical considerations before reaching risk management conclusions (*12*). The approval of research protocols should include guidance on how to keep or destroy the developed materials, and the criteria that should be applied before taking a final decision. Scientists for their part should play an active role in decision-making in order to protect intellectual rights and participate in determining the benefits and risks of the research to be undertaken, including protection and access to VBM. Only a well-structured dialogue involving researchers, the biosafety committee and facility managers may ultimately allow a facility to be adequately prepared to best mitigate the consequences of biosecurity breaches that may also result in external criticism.

However, even though biosafety and laboratory biosecurity are in most respects compatible, a number of potential conflicts exist that need to be resolved.

Figure 1. **Biohazard warning sign for laboratory doors**

Conflicts

In the absence of careful implementation, various aspects of biosafety may conflict with laboratory biosecurity. For example, controls that reduce unauthorized access might also hinder an emergency response by fire or rescue personnel. Mechanisms need to be established that allow entry by emergency responders but ensure uninterrupted and constant laboratory biosecurity, control, accountability and traceability of VBM. Likewise, staff members must be able to quickly and safely exit a laboratory during an emergency without at the same time allowing unrestricted access to sensitive VBM.

Signage may also represent a potential conflict between biosafety and laboratory biosecurity. In the past, biohazard signs placed on laboratory doors identified the biological agents present in the laboratory. However, as a laboratory biosecurity measure to better protect sensitive VBM, LBM3 now recommends limiting the information on biohazard signs to the laboratory biosafety level, the name and telephone number of the responsible investigator, and emergency contact information (*Fig. 1*).

3. The biorisk management approach

Based on a documented agent-based biorisk assessment that includes laboratory biosecurity considerations, laboratories containing VBM should develop systems and controls to provide the required degree of assurance that biosafety and laboratory biosecurity risks are appropriately managed, and that the consequences of release of any VBM from the laboratory are appropriately minimized. Managing these risks represents:

1. reducing the risk of unintentional exposure to pathogens and toxins or their accidental release (biosafety), and reducing the risk of unauthorized access, loss, theft, misuse, diversion or intentional release of VBM to tolerable, acceptable levels (laboratory biosecurity);
2. providing assurance, internally and externally (facility, local area, government, global community, etc.), that suitable measures have been adopted and effectively implemented;
3. Providing a framework for continuous awareness-raising for biosafety, laboratory biosecurity and ethical code of conduct, and training within the facility.

The present document does not provide prescriptive guidance on the development of laboratory biosecurity measures, but describes recommendations and performance expectations, placing responsibility on national authorities and facility managers to demonstrate that appropriate and reasoned biorisk minimization procedures have been established and will be implemented. These recommendations do not call for compliance with a set of requirements, but rather help to identify and set goals to be achieved. This approach allows countries and facility managers to define and choose appropriate systems and controls to ensure that the biorisk management goals that have been identified are reached. It allows institutions to adapt their laboratory biosecurity plans to their particular situation.

3.1 Choice of the expression "laboratory biosecurity"

The term “biosecurity” has been used in different contexts and has acquired different meanings (veterinary health (*13*),[1] ecology,[2,3] agriculture,[4]

[1] The exclusion, eradication and effective management of pests and unwanted organisms in New Zealand (www.pce.govt.nz/reports/pce_reports_glossary.shtml).

[2] Protection of all natural resources from biological invasion and threats (www.hear.org/galapagos/invasives/glossary.htm).

[3] A biosecurity guarantee attempts to ensure that ecologies sustaining either people or animals are maintained. This may include natural habitats as well as shelter and productive enterprise (especially agriculture) and deals with threats such as biological warfare or epidemics. This is related to the more passive concept of biosafety (en.wikipedia.org/wiki/Biosecurity).

[4] Precautions taken to minimize the risk of introducing an infectious agent into a population (www.fao.org/DOCREP/005/AC802E/ac802e0l.htm).

food supply (*14*),[5] arms control, public health (*15*), etc.) for people with different backgrounds. Likewise, the term "biosecurity" is inconsistently translated into various languages. The definition of "laboratory biosecurity" used in this document was developed by WHO in collaboration with FAO and OIE. It restricts the use of the word "biosecurity" to laboratory environments.

The concept of laboratory biosafety has been introduced and discussed in various publications and been the subject of activities as early as the 1960s, and it has become part of an integrated biosafety culture in many countries. In the context of public health, laboratory biosecurity expands laboratory biosafety into a complementary dimension.

3.2 The biorisk management culture

One of the goals of the biorisk management approach is to develop a comprehensive laboratory biosafety and biosecurity culture, allowing biosafety and biosecurity to become part of the daily routine of a laboratory, improving the overall level of working conditions, and pushing for expected good laboratory management.

Role of laboratories

Laboratories are used for clinical medicine, research, the development of pharmaceutical products, the diagnosis of diseases and the confirmation of biological findings. Laboratory-acquired infections should no longer be considered acceptable, no infection or disease should be the result of a breach in biosafety or biosecurity resulting from unsafe or insecure laboratory work practices.

Along with their diagnostic, research and pharmaceutical production capabilities, those working in biological laboratories have unwittingly become partners sharing in the moral responsibility to ensure that the materials they handle are accounted for and secured, and consequently in the protection of global public health. Indeed, biological laboratories in which biorisks are inappropriately managed and the staff and environment exposed to biosafety and biosecurity risks represent a threat to the international community and global public health.

While some facilities may be in a position to know which VBM they handle, work with or store, other facilities receiving for example samples for disease diagnosis or other analyses may not have complete oversight of materials handled. These latter facilities should establish a mechanism to enable either the storage of samples under appropriate conditions, or the destruction of samples once analysis is performed. The adoption of a

[5] "Biosecurity" refers to the policies and measures taken for protecting a nation's food supply and agricultural resources from both accidental contamination and deliberate attacks of bioterrorism. Bioterrorism might include such deliberate acts as introducing pests intended to kill food crops; spreading a virulent disease among animal production facilities; and poisoning water, food and blood supplies (www.ourohio.org/neigh/htmlne/laf_f_abc.php).

comprehensive biorisk management approach should help these facilities to accomplish their duties appropriately.

Minimizing biorisks

Comprehensive biorisk assessments and their results should help laboratories containing VBM institute systems and controls to provide the required degree of assurance that biosafety and laboratory biosecurity risks are appropriately identified and managed, and that the consequences of accidental or intentional release of any VBM from these laboratories are taken into account. Consequences of release should be evaluated by examining the health impacts on the population (death and illness), economic loss, the functional impact on the institution or facility, the impact on the security of other assets, and the impact on public behaviour. Understanding risks and the uncertainties involved is critical for responsible biorisk management. The availability of vaccines, other preventive measures and treatments are important factors in minimizing the consequences of natural or intentional releases of biological material.

Guidance on considerations for performing laboratory biosecurity risk assessments is provided below.

4. Biorisk management

4.1 Securing valuable biological materials (VBM)

Laboratory biosecurity is more than just the safeguarding of dangerous pathogens and toxins from individuals or organizations who would use them for harm. While protection of dangerous pathogens and toxins is obviously appropriate, the scientific, medical and pharmaceutical communities should also consider protecting materials with historical, medical, epidemiological, commercial or scientific value. These decisions should be taken with due consideration to the fact that scientists serve only as temporary custodians of valuable scientific assets whose past and current value to science may be understood, but whose utility for the future can only be estimated.

Some VBM have intrinsic value and they need to be preserved for study by future generations of scientists. Their transfer and sharing should be encouraged or maintained as long as appropriate documentation allowing to track them is available. Thus scientists have a duty to maintain VBM according to current best practice. If a decision is taken to destroy unwanted or unnecessary materials, protocols must be followed to ensure their full and complete destruction and documentation. The protection of VBM includes appropriate storage conditions, documentation of their storage, use, transfer to more appropriate laboratories, or proof of complete destruction.

The classification of biological materials as VBM should be left to their caretakers (laboratory managers and scientists) who should know and understand their value and should be able to address and define the level of protection required. To address these issues, the caretakers of VBM should consult with partners, e.g. in the research community and in the security, intelligence or information technology (IT) sectors to ensure the protection of their valuable assets against identified biorisks. If the facility holding the collection cannot ensure its protection, the laboratory manager together with the responsible scientist(s) should make arrangements to safely transfer them to a more secure site. In this way, policy-makers, scientists, laboratory directors and security engineers, supported by journal editors and publishers of research results, may achieve an appropriate balance between the protection of VBM and the preservation of an environment that promotes legitimate microbiological research.

All microorganisms, natural or laboratory-modified, may be included in the broad definition of VBM. Although some agents have heightened capacities to cause harm if intentionally misused, virtually all may have legitimate uses for medical, commercial and scientific applications. Their value should prompt a responsibility to limit opportunities for VBM to be inappropriately accessed while at the same time preserve opportunities for their study and legitimate use, e.g. for the development of improved vaccines, diagnostics and therapies, work that requires handling, using, transporting, transferring and sharing of VBM.

4.2 Distinctions within VBM

Although all materials of a biological nature may fall within the definition of VBM, in fact not all VBM warrant exceptional protective measures or strict accounting. Indeed, the value of VBM themselves may be based on subjective assessments resulting in biorisk management measures that may differ between sites holding the same agents. In addition, in the diversity of laboratory environments, VBM can often be found in many locations, quantities, processes and materials that may not require accurate quantitative accounting procedures.

Microorganisms are ubiquitous, they are often self-replicating and can thrive under adverse conditions. Unlike chemicals or nuclear materials, they cannot be readily detected and quantified. Minuscule amounts may have high impact on public health status. Given the appropriate conditions, live microorganisms can be multiplied a million-fold in a matter of hours.

In many biological laboratories, only a small subset of VBM may be of high enough value or potential consequence to require detailed accountability or audit measures and substantial economic investment. However, laboratory biosecurity measures should not hamper the ability to work with, share and use of them. VBM may be categorized as follows.

Collections and reference strains

The majority of laboratory-derived materials fall into this group. Laboratory managers and scientists directly responsible for their safekeeping should assess their relative scientific importance to ascertain whether these materials need to be maintained, protected and accounted for. Materials contained within this group may be divided into: (a) collections, strains, biological specimens or materials that have features worth preserving; and (b) ad hoc collected materials.

The first group refers to microbiological cultures, individual isolates, patient specimens (serum, tissue, etc.), cell culture lines, extracted proteins and products that are valuable and necessary for use by the laboratory or have national and international applications. Within this group are included: reference strains and materials indispensable for maintaining quality control (e.g. standards for antibiotic sensitivity and biochemical reactivity, serology standards), strains and materials that have unique characteristics and features (see below); collections that contribute to microbiological diversity (zoonotic agents isolated from diverse hosts and sources, geographical representation and divergent disease manifestations in livestock, humans, wild/domestic birds, representative normal flora microorganisms); strains of epidemiological importance (isolates that represent the evolution of pathogenic features, isolates associated with the spread of a disease agent). Materials whose features were studied and published in journals should be preserved to allow access by scientists wishing to explore, validate and add to the body of knowledge. Materials whose existence poses a threat to people, agriculture, livestock and the environment should be highly protected against diversion

and misuse, or destroyed. Candidates for destruction include replicates of isolates no longer used, materials that have not been stored properly and materials no longer viable, potent, uncontaminated or labelled.

Most cultures, collections and materials are of an ad hoc nature, preserved in laboratories for their temporal and individual value and assembled to meet the interest of the collector(s) or "creator(s)". They take up space and are typically not archived nor cared for once their collector or “creator” has performed the requested analyses, has changed interest topics or has departed from the facility. Their provenance, scientific and economic value may require time to evaluate but they will probably be judged to have no value beyond their original purpose, and thus should not be considered as VBM requiring additional protection. They should be inactivated and discarded or destroyed.

Pathogens and toxins

The group of agents that have received most attention, and indeed require protection in the context of laboratory biosecurity, are pathogens and toxins. They are an important subset of VBM. Pathogens are natural or genetically engineered biological agents that may cause epidemics or pandemics. Toxins are poisonous substances produced by living cells or organisms. Pathogens and toxins are potentially capable of having a mild to severe impact on public health and public health services and may cause social disruption and economic damage.

Pathogens and toxins that have been associated or identified with their use as biological weapons fall into this category. A number of these agents are found naturally in endemic foci around the world, and an unknown number of biological laboratories may be holding them in various forms collected and worked on as part of their routine operations. The potential these agents may represent for harmful or unethical/inappropriate purposes at the global level has been highlighted in recent years. Consequently, laboratories holding them should address the dual-use nature of such agents and take responsibility, following their national guidelines, for deciding on the adoption of appropriate biorisk management measures to protect them from unauthorized access, loss, theft, misuse, diversion or intentional release.

Moreover, global progress in the field of biotechnology has increased the potential for the development of genetically engineered pathogens that express enhanced or unique virulence properties (*12*). This is of concern as highly virulent and highly resistant organisms may be constructed for which there may be no known effective treatment for exposed and infected persons or animals. Recognizing this, the World Health Assembly in 2002 called upon WHO to strengthen public health preparedness for the *deliberate* use of biological agents for harm (*16*). Additional guidance on these issues is provided in *Public health response to biological and chemical weapons, WHO guidance*, second edition, 2004.

Vaccines and other pharmaceutical products

Another significant group of VBM with respect to laboratory biosecurity are the microbial strains used for the development and production of vaccines and other biopharmaceutical products. These strains may be of both public health and commercial value. Strains developed and used to protect the public should be accurately maintained, protected, secured and accounted for. Their destruction, if warranted, should be appropriately documented. Particular attention should be devoted to the increasingly common dual-use of bioregulators (*12*), small biologically active compounds to which the equilibrium of an organism's immune, nervous and endocrine system may be particularly vulnerable.

Food products

For centuries, microbial agents have been used for the development and production of food products, for example to improve bakery, dairy and brewing processes. Mainly yeasts and bacteria fall within this group. Their industrial and economic value may require that they are accounted for and preserved. FAO provides additional guidance on biological risk management in food and agriculture (*17*), a different application of the concept of biosecurity (*not* laboratory biosecurity).

Genetically modified organisms (GMO)

Biotechnology and genetic engineering have been successfully used to construct "de novo" viable viruses (*18*), to enhance the desired properties of microorganisms for public health (diagnostics, vaccines), clinical applications (gene therapy, antimicrobials), agriculture (disease-resistant crops, vector control) and commercial purposes. These include increased quality and quantity of products, enhanced resistance against biological and chemical agents as well as adaptation to growth in hostile environmental conditions. These same technologies may also be employed to increase the virulence of pathogens, or used to modify the resistance of pathogens to existing prophylaxis and treatments. The transfer of genetic materials is commonly associated with methods that impart a preferential selective factor to identify the transgenic recipient. An example is the common selective factor for drug resistance. This drug resistance may under dual-use become a potent biological weapon. Consequently, GMOs are subject to specific oversight through the Convention on Biological Diversity (*19*) and its Cartagena Biosafety Protocol (20), or the Biological and Toxin Weapons Convention (*3*), for their production, use and dissemination.

Non-pathogenic microorganisms

Non-pathogenic microorganisms comprise the group of microbes for which no harmful health-related features are noted naturally. The term typically refers to organisms that are part of the normal flora colonizing specific biological niches and that performs beneficial functions for its host or environment or is not known to cause disease upon

infection. Such organisms may, intentionally or not, acquire pathogenic features under natural or manipulated environments. Microorganisms from this group have been studied and selected representatives have become, as described above, unique strains, working strains, or strains with specific characteristics. Non-pathogenic organisms have been used as hosts for genetic manipulations, scientists using widely accepted methods have created chimeric bacteria or viruses (in effect, GMOs). Therefore, non-pathogenic organisms that are deemed important should be protected against the risk of loss, carefully safeguarded and responsibly maintained.

Extraterrestrial samples

Owing to rapid and increasing developments in the aerospace industry, and to the curiosity of mankind, VBM may also include biological/geological samples taken from other planets and transported to Earth. The uniqueness of such agents or samples, and the potential health and biological risks their release represents, are compelling reasons for them to be safeguarded, protected, accounted for and appropriately secured.

Cellular components and genetic elements

DNA and/or RNA, containing the genetic instructions specifying the biological development of all cellular forms of life including viruses, may be legitimate members of the VBM family. Today's technology allows for the "parent-less" generation of infectious viral particles (e.g. parvoviruses, polioviruses, influenza viruses, etc.). Using only their genetic code, available to researchers with access to published files, biotechnological techniques and reagents, it is possible to reconstitute replicating viruses. The size of DNA molecules and the details of their sequences should help determine their values as VBM. Similar considerations apply with respect to other genetic elements and cellular components.

Radiolabelled biological compounds

The tracing of specific cellular elements and compounds, the identification of specific biological reactions, the elucidation of cellular pathways, but also the diagnosis of non-infectious diseases and many other applications are possible through the use of radiolabelled compounds. Given the half-life of commonly-used radionuclides, ranging from ^{2}H, ^{3}H, ^{32}P, ^{35}S, etc., to ^{137}Cs and others, and the possible consequences of the emitted radiation, specific precautions should be taken to minimize exposure to these elements and to appropriately store and dispose of them.

5. Countering biorisks

5.1 Accountability for VBM

While it is difficult to mitigate the consequences of theft of VBM, i.e. possible misuse, diversion, etc., especially after they have left a given facility, it is easier to minimize such consequences by establishing appropriate controls to protect VBM from unauthorized access or loss. Unauthorized access is the result of inappropriate or insufficient control measures to guarantee selective access. Losses of VBM often result from poor laboratory practices and poor administrative controls to protect and account for these materials. It is important to establish practical realistic steps that can be taken to safeguard and track VBM. Indeed, a comprehensive documentation and description of VBM retained in a facility may represent confidential information, as much as records and documentation of access to restricted areas. However, such documentation may prove useful for example to help discharge a facility from possible allegations. For useful reference, it is recommended that such records be collected, maintained and retained for some time before they are eventually destroyed.

Specific accountability procedures for VBM require the establishment of effective control procedures to track and document the inventory, use, manipulation, development, production, transfer and destruction of these materials. The objective of these procedures is to know which materials exist in a laboratory, where they are located, and who has responsibility for them at any given point in time. To achieve this, management should define:

1. which materials (or forms of materials) are subject to material accountability measures;
2. which records should be kept, by whom, where, in what form and for how long;
3. who has access to the records and how access is documented;
4. how to manage the materials through operating procedures associated with them (e.g. where they can be stored and used, how they are identified, how inventory is maintained and regularly reviewed, and how destruction is confirmed and documented);
5. which accountability procedures will be used (e.g. manual log book, electronic tables, etc.);
6. which documentation/reports are required;
7. who has responsibility for keeping track of VBM;
8. who should clear and approve the planned experiments and the procedures to be followed;
9. who should be informed of and review the planned transfer of VBMs to another laboratory

Accountability does not necessarily imply the identification of exact quantities of biological materials. Living replicating organisms may vary in quantity and quality over the course of laboratory activities and time, and knowing the exact quantity of organisms at any given time is generally not realistic. Moreover, with some biological materials, any amount may be considered significant and relevant. However, biological

materials that are confined to particular containers should be tracked as discrete items. For example, it is possible to maintain an inventory of frozen stocks and an access log to many forms of stored materials. These forms of records are useful as a means of knowing permanently where VBM are located and who has responsibility for them. Records should be secured and easiliy identified, legible and traceable to the activities described. Any changes in biosecurity protocols or equipment and operations should be introduced following clear and documented change-management processes.

Accountability also means ensuring that materials are properly safeguarded. A person(s) with expert knowledge of the material in use and its storage should be accountable. Any anomalies seen by the employee should be promptly reported to the laboratory manager.

5.2 Potential misuse of bioscience

Bioscience research has contributed to the progress of humanity through the development of new vaccines and drugs, and to an improved understanding of human health. However, bioscience has the potential to harm if misused, i.e. the biosciences are inherently dual-use. Although the vast majority of applications of bioscience have been used for good and peaceful purposes, the potential for harmful misuse may suggest the need for specific protective measures for laboratory facilities, the VBM they contain, the work performed, and the staff involved. Biological research is essential to the development of modern health care, public health, agriculture, medicine, veterinary medicine, food production and life science. Products of biological research benefit many economic and social sectors and have the potential for enhancing the health and welfare of virtually every human being.

However, the potential misuse of the biosciences represents a global threat that requires a balanced approach to laboratory biosecurity, acknowledging both its risks and benefits. Such a balanced approach strives to protect the valid role and function of biological laboratories while safeguarding the VBM they may contain. A possible approach to minimizing the dual-use of materials and equipment within a facility is to give a competent biosafety and laboratory biosecurity manager the responsibility for the scientific programme, in consultation with the principal investigator, for approving research projects and authorizing experiments, in compliance with national requirements and bioethical considerations. The role of the institutional biosafety committee and of the research manager in this context is described below.

5.3 Legitimate research, codes of conduct and codes of practice

The advances of science open doors to infinite possibilities to make use of acquired knowledge and techniques (*9*). National authorities and laboratory managers should be able to provide for a legislative and/or regulatory framework defining legitimate and ethical research projects and keep an oversight on laboratory activities and personnel. Systems and controls should be in place to avoid illegitimate or unethical research.

Researchers, laboratory workers and biosafety and laboratory biosecurity managers should communicate and collaborate, and strive to find the correct ethical balance for the activities performed. A voluntary code of conduct can be more effective than one that is imposed provided it is understood and agreed among stakeholders.

The code of conduct should involve evaluation of the purpose of the work, consideration for its impact the publication of research results, and enumerate considerations and conditions for or against the publication of results that may have dual-use implications (*21*). In 2001, a research team backed by a federal grant in Australia created a genetically engineered mousepox virus unexpectedly capable of evading vaccine-induced immunity (*12*). Although the results of the research are not criticable, the publication of the research details has generated strong debates worldwide. Comprehensive bioethical reviews should be carried out and documented before final decisions are reached on the publication of data, balancing pros and cons of their dissemination.

As one example, influenza viruses of the subtype H1N1 that had been the cause of the 1918-1919 pandemic were reconstructed in 2005 from tissues of recovered permafrost-preserved victims and used in BSL3 containment laboratories for pathogenicity studies. Further studies are now planned to combine the genes of the H1N1 pandemic virus with the highly pathogenic H5N1 to investigate virus transmissibility and hopefully be better prepared for a new pandemic. The balance between the lessons one can learn from those studies and the risks of synthesizing potentially new deadly viruses may be argued, but bioethical considerations, international review and control of this research should be extensively examined. There is for example no international agreement, other than specifically for variola virus DNA fragments, that stipulates which sequences may be handled in a laboratory without notification or without specific authorization, and there is no international agreement on what kind of biosafety containment level and laboratory biosecurity practices should apply for specific situations (*22*). These decisions should be left with national or international biosafety-biosecurity-bioethics committees, who should request laboratory managers and laboratory workers to take a responsible risk management approach, and show proof thereof. Only open debates, transparency and documented reasoning may help gain the support of the global community.

Natural risks

Biorisks are not confined only to adverse events related to the accidental or intentional release of VBM. Risks are also represented by natural disasters, threatening the containment and laboratory biosecurity of laboratories in regions at geological risk (earthquakes, hurricanes, floods, tsunamis, etc.). When constructing or maintaining laboratory facilities in such regions, the possible negative outcomes of release of VBM during natural adverse events should be considered, and acceptable biorisk management provisions should be planned.

Transport of materials

The use and storage of VBM should be limited to clearly identified areas. The only VBM permitted outside a restricted area should be those that are being moved from one location to another for specific, authorized reasons. Transport security endeavours to provide a measure of security during the movement of biological materials outside of the access-controlled areas in which they are kept until they arrive at their destination. Transport security applies to biological materials within a single institution and between institutions. Internal material transport security includes reasonable documentation, accountability and control over VBM moving between secured areas of a facility as well as internal delivery associated with shipping and receiving processes. External transport security should ensure appropriate authorization and communication between facilities before, during and after external transport, which may involve the commercial transportation system. The recommendations of the United Nations Model Regulations for the Transport of Dangerous Goods (*23*), providing countries with a framework for the development of national and international transport regulations include provisions addressing the security of dangerous goods, including infectious substances, during transport by all modes.

Transfer of materials

Many countries request to file import and export permits for biological materials before the transfer of such specimens is authorized. These procedures allow for registering and tracking of materials entering or leaving a country, and they are particularly important in the case of alien or dangerous pathogens.

In some instances, stakeholders may deem their collections of VBMs so valuable to warrant the secure storage of a duplicate set in a different location. In such cases, transfer notifications should be established and their access secured.

6. Laboratory biosecurity programme

A comprehensive laboratory biosecurity programme involves:

1. identification of VBM
2. associated agent-based microbiological risk assessment and laboratory biosecurity risk assessment
3. bioethical and scientific analysis of research projects before they are authorized
4. allocation of responsibilities and authorities among staff and facility managers
5. communication between parties involved
6. development of and training on emergency plans; and
7. tailored biosecurity training for employees of the facility and for external first-responders.

All these steps should be the result of a transparent and documented reasoning process that carefully evaluates the impact of biorisk management breaches, and prepares and plans for worst-case scenarios. Individual components of this programme are described below.

6.1 Laboratory biosecurity risk assessment

While the backbone of the practice of biosafety is a microbiological risk assessment, effective laboratory biosecurity programmes should, in addition, perform appropriate laboratory biosecurity risk assessments, followed by the development, approval and endorsement of strategies for their management. Assessment of the suitability of personnel, training and adherence to VBM protection procedures are tools that may be used to achieve these goals. It is important that these biorisk assessment efforts be regularly re-evaluated in an ongoing programme to respond to the requirements of national and institutional standards.

A competent scientific manager should be responsible for managing the scientific programme within the facility. The scientific manager should make sure that appropriate risk assessments for research projects have been performed and cleared, and all records thereof are securely kept; that work is performed according to plan or only with authorized deviations from original plans; that management systems, procedures and records are properly maintained. Assessment timing and scope, describing situations requiring a risk assessment to be carried out or an existing assessment to be re-evaluated, should also be clearly defined and adhered to.

In the context of a biosecurity risk assessment, security and intelligence forces play the fundamental role of complementing the biosafety risk assessments performed by the laboratory management with local threat assessments. Collaboration between these different stakeholders and proactive clarification of their roles, responsibilities and authorities should help in case of emergencies, where first-responders need the appropriate information, knowledge and skills to provide the most appropriate interventions (*Fig.2*).

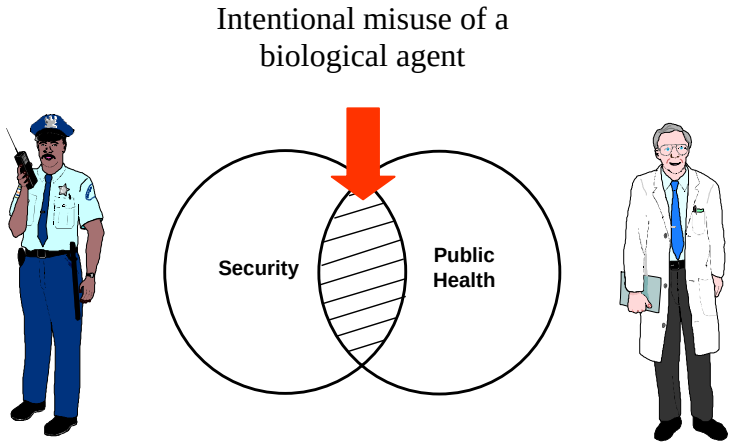

Figure 2. **First-responders: different roles, responsibilities and authorities**

Assessment timing and scope, describing situations requiring a risk assessment to be carried out or an existing assessment to be re-evaluated, should also be clearly defined and adhered to.

6.2 Responsibility for VBM

Laboratory biosecurity should mainly be based on:

1. control and accountability for VBM
2. defining their storage location
3. describing and scrutinizing their use; identifying personnel (and visitors) who should be granted access to them
4. documenting their transfer
5. certifying their inactivation and disposal, and
6. sharing this information with appropriate counterparts within the facility.

Laboratory biosecurity measures should be adapted to the needs of the institutions or facilities adopting them. Their identification should be the result of a biosecurity risk assessment that includes input from scientific personnel and laboratory management, biosafety officers, maintenance staff, IT staff, administrators and law-enforcement representatives.

Local law enforcement may be the police or other local, regional or national security force that is trained to manage security issues. Facilities that handle dangerous pathogens and toxins should ensure that all emergency response personnel, including local law enforcement, are aware of the safety issues on-site and the procedures to be followed if an incident occurs.

The facility should establish a clear working relationship with the local law-enforcement agency to provide a response to security incidents on-site. A clear protocol

should be drawn up detailing the circumstances under which law-enforcement personnel may be summoned, the protocol to follow once on-site, and the scope of authority for all parties involved. Regular on-site training and orientation for the local law-enforcement agency is also recommended.

At facility level, it is recommended that the ultimate responsibility for VBM should lie with the laboratory/facility manager or director, who should be responsible for providing the appropriate conditions to minimize breaches in biosafety and laboratory biosecurity. The facility manager may delegate this responsibility to the principal investigator for routine activities. However, the facility manager will respond in case of biosafety or biosecurity breaches.

At international level, national authorities should be ultimately responsible for breaches in biosafety and laboratory biosecurity that may be at the origin of public health emergencies of international concern (*24*).

6.3 Elements of a laboratory biosecurity plan

Laboratory biosecurity should specifically address the policies and procedures associated with physical biosecurity, staff security, transportation security, material control and information security. It should also include emergency response protocols that address security-related issues, such as specific instructions concerning when outside responders may be called (fire brigade, emergency medical personnel or security personnel), including the protocol to follow once on-site and the scope of authority of all parties involved. It is important for the laboratory security plan to anticipate the most likely situations that would require exceptional access. Just as training is essential for good biosafety practices, it is also essential to train for good biosecurity practices, particularly in emergency situations. Hence regular training of all personnel on security policies and procedures helps ensure correct implementation.

Laboratory biosecurity describes both a process and an objective that is a key requirement for public health and welfare. It requires consideration of the reason for developing regulations, what the objects of the regulations are, how regulations are written, who develops regulations, and who pays for their development and application.

It includes the generation and sharing of scientific knowledge, and involves bioethical considerations such as transparency of decision-making, public participation, confidence and trust, and responsibility and vigilance in protecting society. Effective laboratory biosecurity is a societal value that underwrites public confidence in biological science (*17*).

Securing laboratory equipment

Although laboratory biosecurity mainly focuses on protection of VBM, safeguarding laboratory equipment from unauthorized access, misuse or removal is an important

aspect of laboratory biosecurity that should also be addressed. In biological laboratories, this responsibility lies with the facility managers, the principal investigators and the laboratory staff: all laboratory personnel have a responsibility to take reasonable precautions against theft or misuse of such equipment. Such responsibilities should be clearly outlined in the biorisk management protocol of a facility. On the other hand, security measures for laboratory equipment should be commensurate with the potential risks and imposed in a manner that does not unreasonably hamper research or access to these assets.

As for VBM, not all pieces of laboratory equipment have comparable sensitivity or the same potential for dual-use. Some equipment, e.g. bioreactors, incubators, aerosol disseminators or aerosol test chambers, are among those that may conceivably be used for both legitimate and illegitimate purposes. Specific and detailed laboratory biosecurity measures, procedures and practices may mitigate the risks of their inappropriate use.

Physical biosecurity

Physical biosecurity, comprised of engineering, structural and security personnel elements, is intended to select, control and document access to laboratories and to the materials they contain, and to limit improper removal of VBM and equipment. Access controls are used to limit access to restricted areas to individuals who have proper authorization and to keep track of traffic in and out of these areas. Physical biosecurity measures may become more stringent and more costly as the value of the assets increases and as the location of the materials to be protected is approached.

Personnel management

Personnel management procedures should define the roles, responsibilities and authorities of laboratory personnel who need to handle, use, store, transfer and/or transport VBM, and the manner in which the organization ensures that individuals are appropriate for the positions they hold. These procedures should clearly describe and document the training, experience, competency and suitability requirements for individuals who have access to VBM, ensuring that members of the workforce have appropriate personal and technical qualifications and skills. Documented procedures for the recruitment of personnel should be clearly established and followed. The professional and bioethical eligibility and suitability for working with VBM of all personnel who have regular authorized access to sensitive materials is also central to effective laboratory biosecurity risk management.

A mechanism should be developed to ensure that the integrity of the facility will not be compromised through the absence of key individuals. Such a mechanism should include succession planning for management, scientific, technical and administrative personnel to ensure that critical knowledge of safe and secure operation of the facility does not reside with a single individual, in the event of his/her unavailability or departure. Documented procedures for dismissal of personnel to be disallowed access

to the facility should be developed. Provisions describing personnel management should also address procedures and training for visitors, contractors, subcontractors, suppliers, cleaning and maintenance staff.

Information security

Information security establishes prudent policies for handling sensitive details on VBM. Examples of sensitive information may include laboratory security plans and inventories, and storage locations of VBM. Information security should ensure that the required and appropriate level of confidentiality is preserved by the system that is used to acquire, store, manipulate and manage information.

It is important to establish practical realistic steps that can be taken to safeguard and track VBM. A comprehensive documentation and description of VBM represents the caretaker role of the current laboratory managers to accurately pass on the historical archive of VBM. Some of the information may be confidential but should be available for use by future generations. Such documentation may also prove useful to help discharge a facility from possible allegations.

It is also important to document the existence, location and access to the information for future interests, as security concerns change over time. The objective of information security is to limit access to individuals who have a need to access the information. This may be achieved through marking and secure storage requirements as well as through processes intended to control the manner in which the information is communicated and to whom.

Protection of information should be consistent with the level of risk it poses in terms of potentially compromising a VBM. The higher the level of risk associated with the VBM the institution holds, the greater protection the information associated with the security system will require. Overdoing or exaggerating the sensitivity or level of suspicion can have unintended negative repercussions. This is a difficult process which may require careful consideration and reflection.

Therefore laboratory management and relevant authorities should develop appropriate policies that govern the marking and handling of information and how that information is gathered, maintained, distributed, documented, accessed, shared and stored within the facility and with appropriate counterparts.

Management of laboratory biosecurity activities

Effective laboratory management is a fundamental requirement for both laboratory biosafety and laboratory biosecurity. In order for laboratory managers to be committed, involved and supportive to the safe and secure practice of science, they should bear the responsibility of articulating the need and rationale for both laboratory biosafety and laboratory biosecurity activities. Setting out national performance expectations, i.e. placing responsibility on the facility to demonstrate that appropriate and valid risk

reduction (minimization) procedures have been established, should encourage employees to invest the time and effort required to account for and safeguard the VBM they control. Compliance should be reinforced throughout a facility by the regular use of means to encourage accountability and responsibility (training, scientific meetings, performance reviews, appraisals, codes of conduct/practice, etc.). The requirement to establish a clear biorisk management programme places the responsibility on facility managers to demonstrate that risks are controlled. Only this approach, as opposed to a strict compliance approach, is likely to ensure the commitment and support of managers in the long term, as facility managers should ultimately be held responsible for breaches in biosafety and laboratory biosecurity.

Laboratory biosecurity activities should be established with clear and consistent policies and guidance. These activities should be integrated into the overall policies and administrative procedures of the facility. Managers are responsible for ensuring that biosecurity plans and incident response plans are enforced and revised as needed. Re-evaluation is a necessary and ongoing process since it is unlikely that the range of VBM and threats at any given institution will remain static. Biosecurity programme managers should also conduct biosecurity programme audits (assessments), provide remedial strategies for identified vulnerabilities and gaps, and ensure that the facility's threat and risk assessment is regularly reviewed and updated. Training and familiarization concerning the objectives and requirements of laboratory biosecurity activities should be ongoing.

7. Training

Laboratory biosecurity training, complementary to laboratory biosafety training and commensurate with the roles, responsibilities and authorities of staff, should be provided to all those working at a facility, including maintenance and cleaning personnel, and to external first-responders and responsible staff involved in ensuring the security of the laboratory facility. Such training should help understand the need for protection of VBM and equipment and the rationale for the laboratory biosecurity measures adopted, and should include a review of relevant national policies and institution-specific procedures. Training should provide for protection, assurance and continuity of operations. Procedures describing the security roles, responsibilities and authority of personnel in the event of emergencies or security breaches should also be provided during training, as well as details of security risks judged not significant enough to warrant protection measures. The biorisk management plan should ensure that laboratory personnel and external partners (police, fire brigade, medical emergency personnel) participate actively in laboratory biosecurity drills and exercises, conducted at regular intervals, to revise emergency procedures and prepare personnel for emergencies.

Training should also provide guidance on the implementation of codes of conduct and should help laboratory workers understand and discuss ethical issues. Training should also include the development of communication skills among partners, the improvement of productive collaboration, and the endorsement of confidentiality or of communication of pertinent information to and from employees and other relevant parties.

Training should not be a one-time event. Training should be offered regularly and taken recurrently. It should represent an opportunity for employees to refresh their memories and to learn about new developments and advances in different areas. Training is also important in providing occasions for discussions and bonding among staff members, and in strengthening of the team spirit among members of an institution.

8. Conclusion

Concurrently with the work of other agencies and entities that have addressed biosecurity issues in a variety of contexts and from other viewpoints, this document has addressed VBM and the growing advances in life sciences and related technologies that are likely to alter the spectrum of current and future biorisks, presenting ways to identify, prevent and minimize them.

The biorisk management approach described here is composed of a biosafety, a laboratory biosecurity and an ethical component. It offers laboratory facilities a programme that should help them to account for and protect their valuable scientific assets.

Under the ultimate responsibility of laboratory directors whose tasks should include the ability to demonstrate that risks are appropriately managed, biorisk management programmes may be divided into seven main components:

1. Identify VBM that require protection on the basis of regularly performed biorisk assessments.
2. Establish clear guidance, roles, responsibilities and authorities for those who work with or have access to VBM and to the facilities that contain them.
3. Promote a culture of awareness, shared sense of responsibility, ethics, and respect of codes of conduct within the international life science community.
4. Develop policies that do not hinder the efficient sharing of reference materials and scientific data, clinical and epidemiological specimens and related information, and that do not impede the conduct of legitimate research.
5. Strengthen collaboration between the scientific, technical and security sectors.
6. Provide appropriate training to employees of laboratory facilities.
7. Strengthen emergency response and recovery plans on the assumption that biorisk management systems can only minimize, but never really eliminate, every conceivable threat.

Furthermore, the commitment to constantly improve biorisk management performance for a facility and its operation through attainable goal-setting and actual goal-achieving should be encouraged and acknowledged at all levels.

9. References

1. Organization for Economic Cooperation and Development (OECD) Biosecurity codes (http://www.biosecuritycodes.org/gloss.htm)
2. World Health Organization. *Laboratory biosafety manual*. Third edition. Geneva, World Health Organization, 2004 (http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/).
3. Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction (Biological Weapons Convention), 1975 (http://www.opbw.org)
4. *Enhancement of laboratory biosafety*. World Health Assembly resolution WHA58.29, May 2005 (http://www.who.int/gb/e/e_wha55.html# Resolutions).
5. 2001 Anthrax attacks (http://en.wikipedia.org/wiki/Cases_of_anthrax).
6. Universal Declaration on Bioethics and Human Rights, United Nations Educational, Scientific and Cultural Organization (UNESCO), 2005 (http://portal.unesco.org/shs/en/ev.php-URL_ID=1883&URL_DO=DO_TOPIC&URL_SECTION=201.html).
7. *Smallpox: destruction of variola virus stocks*. Discussion document A58.10, World Health Assembly, May 2005 (http://www.who.int/gb/e/e_wha58.html#Main_documents).
8. *Smallpox eradication: destruction of variola virus stocks*. World Health Assembly resolution WHA55.15, May 2002 (http://www.who.int/gb/e/e_wha55.html#Resolutions).
9. Life science research: opportunities and risks for public health. *Mapping the issues* (http://www.who.int/csr/resources/publications/deliberate/WHO_CDS_CSR_LYO_2005_20/en/).
10. Sundelius B, Grönvall J. Strategic dilemmas of biosecurity in the European Union. *Biosecurity and bioterrorism: biodefense strategy, practice, and science*, 2004, 2(1):17-23.
11. Cook-Deegan RM et al. Issues in biosecurity and biosafety. *Science*, 2005, 308:1867-1868.
12. Jackson RJ et al. Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox. *Journal of virology*, 2001, 75:1205-1210.
13. Food and Agriculture Organization of the United Nations. Biosecurity for agriculture and food production. Introduction to biosecurity, 2003 (http://www.fao.org/biosecurity/).
14. Kelly AM. Veterinary medicine in the 21st century: the challenge of biosecurity. *Institute for Laboratory Animal Research journal*, 2005, 46:62-64.
15. Choch-Spana M et al. Influenza vaccine scarcity 2004-05: implications for biosecurity and public health preparedness. *Biosecurity and bioterrorism: biodefense strategy, practice, and science*, 2005, 3(3):224-234.
16. *Global public health response to natural occurrence, accidental release or deliberate use of biological and chemical agents or radionuclear material that affect health*. World Health Assembly resolution WHA55.16, May 2002, (http://www.who.int/gb/e/e_wha55.html#Resolutions).

17. FAO Technical Consultation on Biological Risk Management in Food and Agriculture, Bangkok, Thailand, 13-17 Jan 2003 (http://www.fao.org/ag/agn/food/meetings_biosecurity_en.stm).
18. Cello J, Paul AV, Wimmer E. Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template. Sciencexpress, 11 July 2002, 10.1126/science.1072266 (http://www.sciencemag.org/cgi/content/abstract/1072266v1)
19. United Nations Environment Programme. Convention on Biological Diversity. Earth Summit, Rio de Janeiro, Brazil, 1992 (http://www.biodiv.org/convention/default.shtml).
20. United Nations Environment Programme. Convention on Biological Diversity. Cartagena Protocol on Biosafety (http://www.biodiv.org/ biosafety/default.asp).
21. Statement on the consideration of biodefence and biosecurity. *Nature*, 2003:421:771.
22. Von Bubnoff A. The 1918 flu virus is resurrected. *Nature*, 2005, 437:794-795.
23. Recommendations on the Transport of Dangerous Goods, Model Regulations. Fourteenth revised edition. United Nations, New York and Geneva, 2005 (http://www.unece.org/trans/danger/publi/unrec/rev14/ 14files_e.html).
24. *International Health Regulations*. World Health Assembly resolution WHA58.3, May 2005 (http://www.who.int/gb/e/e_wha58.html# Resolutions).

10. Bibliography

- Centers for Disease Control and Prevention .US Department of Health and Human Services. Select Agent Program, final rules. Atlanta, Centers for Disease Control and Prevention, 2005 (http://www.cdc.gov/od/sap/final_rule.htm).
- FAO. *Biosecurity in food and agriculture*. Committee on Agriculture. Seventeenth session, Rome, 31 March-4 April 2003. Rome, FAO, 2003 (COAG/2003/9, http://www.fao.org/DOCREP/MEETING/006/Y8453E.HTM).
- FAO/WHO. Biosecurity risk analysis: an overview and framework manual. Chapter 4. Rome/Geneva, 2005, FAO/WHO (draft, May 2005).
- Health Canada. *Laboratory biosafety guidelines*. Third edition. Ottawa, Health Canada, 2004.
- Institute of Medicine and National Research Council. *Globalization, biosecurity, and the future of the life sciences.* Washington DC, The National Academies Press, 2006
- National Institutes of Health/Centers for Disease Control and Prevention. *Biosafety in microbiological and biomedical laboratories.* Fourth edition. Atlanta, CDC, 1999.
- WHO. *Global health security: epidemic alert and response.* World Health Assembly resolution WHA54.14, May 2001 (http://ftp.who.int/gb/pdf_files/WHA54/ea54r14.pdf)
- WHO. *Global public health response to natural occurrence, accidental release or deliberate use of biological and chemical agents or radionuclear material that affect health.* World Health Assembly resolution WHA55.16, May 2002. (http://www.who.int/gb/ebwha/pdf_files/WHA55/ewha5516.pdf)
- WHO. Deliberate use of biological and chemical agents to cause harm. World Health Assembly resolution WHA55.20, May 2002 (http://www.who.int/gb/ebwha/pdf_files/WHA55/ea5520.pdf)