WHO GUIDANCE on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories – a stepwise approach

WORLD HEALTH ORGANIZATION
GENEVA, 2020

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ISBN 978-92-4-151626-6

Suggested citation. WHO guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories – a stepwise approach. Geneva: World Health Organization; 2020.
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Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.
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FOREWORD

This document is the result of a scientific project initiated jointly by the World Health Organization (WHO) and the University of Applied Sciences Lübeck, Germany, and is a direct response to an expressed need for practical information and guidelines designed to support policy-makers and national regulatory bodies develop and strengthen national biosafety and biosecurity regulatory frameworks.

The first draft of this document was based on a detailed analysis of current practice, drawing on a comprehensive review of published documents detailing existing regulatory policies and structures and frameworks in a diverse set of countries. This review examined both primary and secondary legislation, as well as non-legally-binding instruments (standards, guidelines and recommendations) from multiple sectors. The review was conducted by staff at WHO and the University of Applied Sciences Lübeck, Germany.

As part of a pilot exercise, and in order to support the development of biosafety and biosecurity regulations in a country with limited capacity in this area, a first draft of this document was circulated, reviewed and discussed with stakeholders from the Democratic Republic of Ethiopia during July 2018. The valuable feedback received from those involved in the pilot exercise was used to further develop and refine the guidance.

Shortly afterwards, a meeting was held at WHO headquarters in Geneva to review the revised version of the guidance document. The three-day meeting (26–28 September 2018) involved the participation of representatives from WHO Member States, WHO Regional Offices and several international organizations. The views and comments expressed by participants during the in-depth interactive discussions were taken into consideration during the preparation of this final version of the guidance document.

ACKNOWLEDGEMENTS

The World Health Organization would like to acknowledge the following individuals who contributed in a major way to the development of the present guidance document, including the initial review work which led to the first draft: Dr Kazunobu Kojima (WHO Headquarters, Switzerland), Ms Arpitha Rao (University of Applied Sciences Lübeck, Germany), Mr Amit Kumar Chaudhary (University of Applied Sciences Lübeck, Germany) and Professor Folker Spitzenberger (Centre for Regulatory Affairs in Biomedical Sciences, University of Applied Sciences Lübeck, Germany).

This document has benefitted greatly from the contributions and insightful feedback provided by the following experts who participated in the pilot exercise: Dr Tsigerade Kifle (Ethiopian Public Health Institute, Addis Ababa, Ethiopia), Mr Adisu Kebede (Ethiopian Public Health Institute, Addis Ababa, Ethiopia), Dr Abiy Girmay Haddis (WHO Ethiopia) and Dr Aggrey Bategereza (WHO Ethiopia).

The World Health Organization would also like to thank all those who participated in the September 2018 meeting and whose valuable input and review comments have helped to shape the final version of this document: Ms Whitney Arneaud (Caribbean Public Health Agency, Trinidad and Tobago), Dr Giovanni Cattoli (Joint FAO/IAEA Division, International Atomic Energy Agency, Austria), Dr José Alberto Diaz Quinonez (Institute of Epidemiological Diagnosis and Reference InDRE, Mexico), Dr Samuel S. Edwin (Division of Select Agents and Toxins, CDC, USA), Ms Cindy Evans (Public Health Agency of Canada), Mr Niels Kongshøj (Cenre for Biosecuirty and Biopreparedness, Denmark), Ms Yoline Kuipers (European Commission, Luxembourg), Mr Vasilii Kuklev (Russian Research Anti-Plague Institute "Microbe"), Ms Jennifer Lasley (World Organisation for Animal Health (OIE), France), Dr Thuy Nguyen Thanh (National Institute of Hygiene and Epidemiology, Vietnam), Dr Nurbolot Usenbaev (Republic Centre of Quarantine and Dangerous Infectious Diseases, Kyrgyzstan), Dr Mark van Passel (National Institute for Public Health and the Environment, The Netherlands), Dr Svetlana Portenko (Russian Research Anti-Plague Institute "Microbe"), Mr Scott Spence (Committee Established Pursuant to Security Council Resolution 1540, United Nations, USA), Dr Enkhzaya Sukhee (National Centre for Communicable Diseases, Mongolia), Dr Ni Ketut Susilarini (National Institute of Health Research and Development, Indonesia), Dr Harish Chandra Upreti (National Public Health Laboratory, Nepal), Dr Michael Weaver (International Federation of Biosafety Associations, Canada), Dr Yahaya Ali Ahmed (WHO Regional Office for Africa, Congo)*, Dr Jean-Marc Gabastou (WHO Regional Office for the Americas, Mexico), Dr Franciscus Konings (WHO Regional Office for Eastern Mediterranean, Egypt), Dr Evgeniy Gavrilin (WHO Regional Office for Europe, Denmark), Dr Aparna Singh Shah (WHO Regional Office for South-East Asia, India), Dr Karen Nahapetyan (WHO Regional Office for Western Pacific, the Philippines), Ms Lisa Carter (WHO Lyon, France), Dr Sebastien Cognat (WHO Lyon, France), Dr Jacqueline Fournier-Caruana

* Unable to attend but commented.

(WHO Geneva, Switzerland), Dr Florence Fuchs (WHO Lyon, France), Mr Abbas Omar (WHO Geneva, Switzerland), Dr Rajesh Sreedharan (WHO Geneva, Switzerland), Ms Lisa Stevens (WHO Lyon, France).

We also gratefully acknowledge and recognize the major contributions of Ms Cindy Evans (Public Health Agency of Canada, Canada), Dr Christina Scheel (Centers for Disease Control and Prevention, USA), Ms Sonia Drobysz (Verification Research, Training and Information Centre (VERTIC), United Kingdom) and Dr David Franz (former US Army Medical Research Institute of Infectious Diseases, USA).

ACRONYMS AND ABBREVIATIONS

BWC	Biological Weapons Convention
CWA	CEN Workshop Agreement
DURC	Dual-use research of concern
GMO	Genetically-modified organism
GMPP	Good microbiological practices and procedures
IHR	International Health Regulations
ISO	International Organization for Standardization
NBBC	National biosafety and biosecurity committee
NBBF	National biosafety and biosecurity regulatory framework
NRA	National regulatory authority
OIE	World Organisation for Animal Health
SSBA	Security sensitive biological agent
UN	United Nations
UNCETDG	United Nations Committee of Experts on the Transport of Dangerous Goods
WHA	World Health Assembly
WHO	World Health Organization

SECTION 1

INTRODUCTION

1.1 Background

The concepts of biosafety and biosecurity are central to efforts to protect human health against the risks posed by exposure to hazardous biological agents. Biosafety, a term used to describe the collection of technologies, processes and practices aimed at preventing the unintentional exposure to biological agents, has in particular accrued increasing importance in recent decades as a result of the trend towards globalization and concomitant growth in international communication, transport and trade. In this international context, the outbreaks of highly-infectious diseases that have occurred in the last years serve to underscore the urgent need for effective prevention, detection and response to biological risks, in accordance with the International Health Regulations (IHR) *(1)*.

Since they play a key role in ensuring that all biological agents are correctly identified and safely handled in accordance with best practice regulations, biomedical laboratories are considered to be fundamental agents of biosafety (and biosecurity). Biomedical laboratories can also have an important part to play in building in-country biological risk management capacity and promoting a culture of responsibility. It is for these reasons that control of biological risks typically begins at the national level, with countries establishing laws and regulations which stipulate the type of control measures that must be implemented if a laboratory is to be authorized to operate. Most countries that have developed such regulatory systems have also established some form of monitoring or oversight mechanism to ensure laboratory compliance with national laws and regulations.

The nature and scope of the regulatory arrangements for assuring biosafety and biosecurity in biomedical laboratories among WHO Member States is currently extremely diverse. Some counties have highly-developed regulatory systems, with detailed legislation backed up by robust networks of regulatory bodies and stakeholders, each with well-defined responsibilities and processes. At the other end of the spectrum, however, there are some countries that almost completely lack regulatory guidance in the field of laboratory biosafety and biosecurity.

There is also a wide variation in the context and primary orientation of regulatory frameworks even among the countries with well-developed systems. Some countries have systems that are geared towards the protection of occupational health while others are focused on the threats to security. Furthermore, many established regulatory frameworks currently lack the necessary flexibility to proactively manage and to respond adequately to risks and situations derived from new technologies and newly-evolving and emerging diseases, especially zoonotic diseases. In addition, biosecurity risks related to the misuse of advanced technologies are often neglected or entirely omitted. Finally, because biosafety and biosecurity are closely linked to issues

related to animal health, environmental protection and the misuse of biological agents, there is a now a greater need for regulatory frameworks to develop more integrative approaches to managing biological risk to ensure they cover a wider range of topics and the full spectrum of potential threats to global public health.

Since 1983 and the publication of the first edition of WHO's Laboratory Biosafety Manual countries have been encouraged to embrace the concept of biosafety and develop national codes of practice for the safe handling of pathogenic biological agents. Now in its fourth revision, WHO's biosafety manual *(2)* continues to provide international leadership in matters related to biosafety and biosecurity. The revised edition, published in 2019, aims to guide sustainable developments in laboratory biosafety – by advocating a greater focus on national oversight systems, worker training, good microbiological practice and evidence- and risk-based assessment ¬in order to promote a responsible safety culture, build country capacity and improve compliance the current IHR *(3)*. However, in focusing on the technical and medical–scientific aspects of laboratory biosafety and biosecurity at the local (i.e. individual laboratory) level, the biosafety manual does not provide systematic guidance on some of the wider issues related to the regulation of the activities of biomedical laboratories from a national perspective. Conversely, guidance documents aimed at policy-makers and regulators do not generally provide sufficient practical information about the activities of biomedical laboratories. This guidance document aims to bridge that gap by addressing the needs of policy-makers, regulators and biomedical laboratories for comprehensive information which supports the development of effective regulatory frameworks for improving biosafety and biosecurity at biomedical laboratories.

1. 2 Intended scope and objectives of this guidance

This document aims to inform and support national legislative and executive authorities, policy-makers and regulators in creating, refining and implementing a regulatory framework for ensuring the highest standards of laboratory biosafety and biosecurity.

In the context of this publication, the term "laboratory biosafety" is used to describe the containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents or their accidental release in biomedical laboratories.

The term "laboratory biosecurity" is used to describe the principles, technologies and practices that are implemented for the protection, control and accountability of biological materials and/or the equipment, skills and data related to their handling in biomedical laboratories. The aim of biosecurity measures is to prevent the unauthorized access, loss, theft, misuse, diversion or release of pathogenic biological agents.

Unless indicated otherwise, the term "regulatory framework" may be interpreted throughout to mean the system of internationally- and nationally-binding legislation and regulations supplemented and specified by voluntary, best-practice standards, guidelines and recommendations.

The term "biomedical laboratories" is used in this document to refer to healthcare, diagnostic and medical laboratories, public health laboratories, veterinary laboratories, research centres, biobanks, pharmaceutical and all other types of facilities that handle or store hazardous biological agents. Other terms used in this document are defined in the attached glossary (see Annex I).

In order to meet its objectives, this document provides recommendations regarding what components or elements a comprehensive and integrated regulatory framework for biosafety and biosecurity would need to incorporate and the enabling conditions that would be required to effectively implement such a framework. To support national authorities in the development of appropriate regulatory requirements, this document incudes a high-level review of existing biosafety and biosecurity regulations in selected WHO Member States (see Section 2 and Annex II), as well as a questionnaire tool to assist users conduct a comprehensive initial situational analysis of existing biosafety and biosecurity controls in biomedical laboratories (see Annex III: Section B).

In order to assist users with the more practical aspects of developing and implementing a comprehensive regulatory system, this document describes some of the frequently encountered challenges and barriers to improving biosafety and biosecurity at the national and institutional level. In keeping with the practical approach adopted by this guidance, it also presents a seven-step plan for developing and implementing laboratory biosafety and biosecurity regulations, as follows:

STEP 1: Mobilize national commitment and resources for the development and implementation of a national biosafety and biosecurity policy

STEP 2: Conduct a national evaluation and surveys

STEP 3: Establish national institutions and operational mechanisms and develop best-fitting regulations

STEP 4: Strengthen expertise to support implementation of a suitable regulatory system

STEP 5: Implement and enforce regulations

STEP 6: Establish national information exchange networks and international partnerships

STEP 7: Review performance and adaptability to the national context and evolving risks

Countries that already have regulations in place for biosafety and biosecurity are encouraged to review their framework regularly, as guided by this document. In this regard, it should be noted that the recommendations made in this document

are intended as guidance only and are not intended to replace existing national or international legislation. Instead, they support a process of continual improvement, the ultimate goal of which is the effective implementation of biosafety and biosecurity legislation that is in compliance with relevant national and international agreements, including the IHR.

1.3 Target audience

This guidance is primarily designed to support the needs of those WHO Member States that have few regulations governing the activities of biomedical laboratories and relatively weak regulatory biosafety and biosecurity systems. Regulators and regulatory authorities form the main target audiences, but other stakeholders – such as ministries of health, agriculture, environment, trade and industry, legislative and executive branches of the government, policy-makers, and standardization organizations – may also find this document useful.

In the context of increasing awareness of the challenges in implementing regulatory requirements at the facility level, biomedical laboratory managers may also benefit from the guidance and recommendations provided in this document. Other laboratory-related organizations, as well as healthcare professionals, academics and researchers working in the field of biosafety and biosecurity may also find aspects of this guidance useful.

1.4 Limitations

This document provides a general approach but does not offer country-specific guidance on the development or implementation of statutory laws and regulations. While detailed guidance on the more legal and technical aspects of laboratory regulations is beyond the scope of this document, it does nevertheless provide references to relevant documents where such information can be found.[1]

This document is written largely for the legislative and executive branches of government and mainly describes the role and responsibilities of a country's regulatory authority in relation to the implementation of an effective laboratory biosafety and biosecurity framework. Although it does not necessarily detail responsibilities of other stakeholders, such as biomedical laboratories professionals, academics, manufacturers, researchers among others, their general and specific roles in carrying out activities related to biosafety and biosecurity should not be undervalued.

While this document provides a concise overview of what might be entailed in developing or enhancing a regulatory framework for biosafety and biosecurity, it does not discuss or attempt to explain in any great detail the available concepts and tools that have been designed in recent years to support such endeavours. Users are therefore recommended to use this guidance document in combination with other analytical and procedural guidance documents and manuals.[1]

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[1] See "Selected further reading"

1.5 How to use this document

This guidance document should be read as a road map for developing and implementing either new or revised legislation related to laboratory biosafety and biosecurity. While it describes a number of components or "elements" that are generally considered to be integral to a comprehensive national biosafety and biosecurity framework (NBBF), this suggested list is intended to be neither exhaustive nor prescriptive. Countries may incorporate all the proposed components into their own regulatory framework as described, or make adaptions to suit their own national and/or local regulatory needs.

The major part of this document is devoted to outlining a seven-step approach to improving biosafety and biosecurity at biomedical laboratories through the establishment of an effective regulatory system (see Section 3). It should be emphasized that as countries are likely to be at different stages in the development of their regulatory environment as it relates to biosafety and biosecurity, the recommended steps might be taken in an iterative, sometimes simultaneous way, and therefore do not necessarily have to be followed in strict numerical order.

Section 3 describes some of the challenges that countries have faced in implementing laboratory biosafety and biosecurity measures and in establishing the enabling conditions for effective regulation in this area. These comments have been included to make users aware of some of the impediments and barriers to effective regulation. In addition, the discussion of each step of the recommended approach includes a summary table which lists a number of key decision points. This list of decision points is designed to assist users carry out each step, and is supplemented with a brief description of some of the approaches currently taken by countries (as policy options), and/or additional issues that may need to be taken into consideration.

This document provides supporting information in the form of a list of "Selected further reading", which readers are encouraged to refer to for more detailed information on topics related to laboratory biosafety and biosecurity. For ease of use, this list of further reading has been subdivided into topic areas. As previously mentioned, Annex II provides a list of laws, regulations and other instruments that have been adopted by selected WHO Member States. Users may like to refer to this list while developing or revising their regulatory frameworks, but should be aware that adopting regulations adopted by other countries with little or no modification, and without national evaluation, is strongly discouraged. Finally, Annex III provides a detailed (self-) assessment tool to guide policy-makers and regulators through the task of developing and implementing a national biosafety and biosecurity regulatory framework using the stepwise approach recommended in this guidance document (see Annex III: Section C).

SECTION 2

REGULATORY FRAMEWORKS FOR LABORATORY BIOSAFETY AND BIOSECURITY: AN OVERVIEW OF CURRENT PRACTICE

Thanks to a series of international initiatives which have increased the profile of biosafety and biosecurity over the last two decades, most WHO Member States have taken steps to regulate the handling, storage and transportation of biological agents within their borders. Consequently, most countries have now introduced some form of regulatory control which addresses biosafety and biosecurity risks at biomedical laboratories. Moreover, it is generally accepted that countries need to have in place a minimum set of regulations that ensure the adoption of good microbiological practices and procedures (GMPP) in all their biomedical laboratories.

Despite broad agreement on the general principles, both the approach to regulation and the regulations themselves differ enormously among Member States. A review of current practice conducted to inform this guidance confirmed that there is wide variation between countries, for example, in the scope and emphasis of their regulatory programmes, as well as in the hierarchy and transparency of their frameworks – especially with regard to the application of risk management concepts to the classification of biological agents (see Annex II). The manner in which countries structure and organize regulatory oversight of their biomedical laboratories is also far from being convergent or comparable across the world.

By way of illustration of the inherent variety in current approaches to biosecurity and biosafety regulation, Table 2.1 lists some of the criteria that are commonly used to characterize a national or regional regulatory framework. The third column of this table describes some of the root causes of gaps in existing regulatory structures and some of the commonly encountered challenges faced by policy-makers and regulators when addressing issues of biosafety and biosecurity through regulation.

This list of criteria may be also considered as a starting point for a conducting preliminary or initial situational analysis of existing biosafety and biosecurity legislation and to this end, for each listed element or criterion, at least one “signalling” question

is provided. These questions are designed to help users identify and describe key characteristics that may or may not be present in an existing regulatory framework. A comprehensive evaluation of existing regulatory arrangements, including the identification of any gaps, forms part of the recommended step-wise approach to implementing a national biosafety and biosecurity framework (NBBF) and is described in more detail later in this document (see Section 3: STEP 2).

Table 2.1 Characterizing national or regional regulatory frameworks for laboratory biosafety and biosecurity: a list of possible criteria (non-exhaustive)

CRITERIA FOR REGULATORY FRAMEWORK CHARACTERIZATION	QUESTION(S)	COMMON CAUSES OF EXISTING REGULATORY SHORTCOMINGS OR CHALLENGES
Hierarchy and structure of the regulatory framework	Are biomedical laboratory activities related to biosafety issues regulated by statutory laws enforced by governmental or nongo-vernmental agencies? Are biomedical laboratory activities related to biosecurity issues regulated by statutory laws enforced by governmental or nongo-vernmental agencies? Does the framework refer to binding primary and secondary legislation (i.e. laws and regulations respectively) or to "soft law" (i.e. non-binding/voluntary standards, guidelines and recommendations)?	No sufficient or adequate legislation for biosafety in place to be applied by biomedical laboratories No sufficient or adequate legislation for biosecurity in place to be applied by biomedical laboratories Requirements for biomedical laboratories are not sufficiently linked to mandatory legal instruments or lack sufficient substantiation by technical guidelines

Table 2.1 Characterizing national or regional regulatory frameworks for laboratory biosafety and biosecurity: a list of possible criteria (non-exhaustive) (continued)

CRITERIA FOR REGULATORY FRAMEWORK CHARACTERIZATION	QUESTION(S)	COMMON CAUSES OF EXISTING REGULATORY SHORTCOMINGS OR CHALLENGES
Scope and emphasis of the regulatory framework	In which legal context are biomedical laboratories currently regulated? For instance, do regulations primarily refer to employee protection, misuse of biological agents, laboratory quality and/or other sectors such as transport? Is there separate or common legislation for biosafety and biosecurity aspects? Do regulations primarily cover naturally- occurring organisms and/or genetically- modified organisms?	Limited or inadequate scope of existing legislation
Profiling of biological agents	Is there any kind of biosafety classification system in use? If yes, is the assignment of microbiological agents to a biosafety level based on a thorough risk assessment? Is a pathogen list periodically updated?	Lack of flexibility of the chosen classification system Lack of evidence- and risk-based perspectives on profiling of biological agents No adequate assignment of responsibilities for periodic review of legislation
Biological agent containment	Does the biosafety level of containment take into consideration procedures, volume and titre on top of profiling of the microbio-logical agent?	Lack of flexibility of the chosen classification and containment system

Table 2.1 Characterizing national or regional regulatory frameworks for laboratory biosafety and biosecurity: a list of possible criteria (non-exhaustive) (continued)

CRITERIA FOR REGULATORY FRAMEWORK CHARACTERIZATION	QUESTION(S)	COMMON CAUSES OF EXISTING REGULATORY SHORTCOMINGS OR CHALLENGES
Organization of regulatory oversight	Is there a mechanism in place to ensure regulatory implementation and oversight of the criteria to be fulfilled by biomedical laboratories? If responsibility for oversight is shared between multiple regulatory bodies, are those responsibilities and interfaces between the institutions well-defined and transparent to the stakeholders? Do the different bodies communicate and collaborate regularly?	Insufficient and unclear assignment of responsibilities for regulatory oversight Insufficient communication strategies between involved agencies, institutions and relevant stakeholders
Registration/ notification system for laboratories	Is there an independent notification system in place which allows the regulator to authorize individual laboratories to work with specific biological agents?	Lack of information and communication systems for laboratory notification
Accident/Incident reporting system	Is a reporting system for accidents and incidents established? Are reporting procedures well-defined and transparent to the stakeholders?	Lack of adequate accident/ incident definition Lack of communication systems for accident/ incident reporting
Risk management system	Are adequate laboratory rules or guidance for performing risk management established?	Insufficient knowledge of risk management tools

Table 2.1 Characterizing national or regional regulatory frameworks for laboratory biosafety and biosecurity: a list of possible criteria (non-exhaustive) (continued)

CRITERIA FOR REGULATORY FRAMEWORK CHARACTERIZATION	QUESTION(S)	COMMON CAUSES OF EXISTING REGULATORY SHORTCOMINGS OR CHALLENGES
Training	Is there a mechanism that ensures proper training of the laboratory personnel proportionate to the assessed risk?	Insufficient training capacities for regulatory and laboratory staff
"One health" approach	Do regulatory requirements and regulatory structures fully address both the human and veterinary health sectors? Are regulatory structures shared between the human and veterinary health sector?	Insufficient communication strategies and inadequate experience exchange between the human and the veterinary health sector
Implementation strategy for laboratories	Is guidance for implementation of the regulatory requirements for biomedical laboratories published, regularly reviewed and effectively communicated to the users at laboratories?	Insufficient communication strategies between regulators and laboratories
Licensing/inspection oversight systems	Is there a requirement for the licensing, inspection and/or registration of biomedical laboratories?	Lack of regulators' knowledge and understanding of the activities of biomedical laboratories

Many countries base their national biosafety legislation on one or more international treaties and agreements, such as:

- the International Health Regulations (IHR) *(1)*
- World Health Assembly Resolutions such as the WHA 58.29 Enhancement of laboratory biosafety *(4)*
- the Cartagena Protocol on Biosafety to the Convention on Biological Diversity *(5)*
- the OIE Terrestrial Animal Health Code *(6)*
- the Manual of diagnostic tests and vaccines for terrestrial animals *(7)*

In the terms of the matter of biosecurity, countries often defer to the following international agreements and conventions:

- the Biological Weapons Convention *(8)*
- the United Nations Security Council Resolution 1540 *(9)*
- the OIE Biological Threat Reduction Strategy *(10)*

While these above-mentioned agreements and instruments are designed to promote the concept of, and need for improvements in, biosafety and biosecurity, they are fairly broad in their scope and in many cases provide insufficient practical guidance for the policy-maker charged with the task of developing a comprehensive set of national polices and laws to regulate the activities of biomedical laboratories. In short, the texts of international conventions and agreements establish the general concepts and principles, but do not cover of the specifics of biosafety and security regulation.

In most countries, regulatory control of biological risk comprises a mix of primary and secondary legislation (i.e. laws, acts, regulations) and so-called "soft" law, that is, non-legally binding guidelines and standards (see Annex II). Several international expert bodies, including WHO and the International Organization for Standardization (ISO), have developed guidelines and standards which cover many different aspects of laboratory biosafety and biosecurity and which have been adopted (with or without adaptation) by individual countries. These international guidelines and standards generally advocate best practice approaches that provide conformity with state-of-the-art technology and scientific knowledge and international agreements, such as the IHR.

Examples of international guidelines and standards include the WHO Laboratory biosafety manual *(3)*, ISO 15190 (ISO's Medical laboratories – Requirements for safety *(11)* and the CWA 15793 (CEN Workshop Agreement on Laboratory Biorisk Management System) *(12)*. The latter has recently been converted so as to make it comparable (but not identical) in scope and content to the ISO standard, ISO 35001. In the context of the "One Health" approach, the Codex Alimentarius *(13)* might be considered as another relevant standard example.

As indicated in the Introduction (see Section 1.1: Background), the above-mentioned international guidance documents are focused on the scientific and technical aspects of laboratory biosafety and biosecurity and do not necessarily address the specific informational needs of policy-makers and regulators, to whom this guidance is directed. The stepwise approach to implementing regulatory requirements for laboratory biosafety and biosecurity described in the following section (Section 3) draws on the real-world experiences of different countries whose regulatory systems are at different stages of development. The initial draft was based on the review of current practice conducted by the lead authors of this guidance. The present, revised version takes into account the lessons learned from a pilot exercise conducted in the Democratic Republic of Ethiopia and the outcome of the discussions of a subsequent review meeting.

SECTION 3

STEPWISE APPROACH TO REGULATING LABORATORY BIOSAFETY AND BIOSECURITY

The stepwise approach to developing and implementing effective regulatory systems with regard to laboratory biosafety and biosecurity recommended in this guidance document comprises seven steps. These seven steps are shown in overview in Figure 3.1 and are described in greater detail in the reminder of this section. It is re-iterated that the recommended steps may be undertaken in an iterative, sometimes simultaneous fashion, and do not necessarily have to be followed in numerical order.

Users are reminded that the primary purpose of regulatory systems is to provide the necessary conditions to enable biomedical laboratories and other stakeholders working in the field of biosafety and biosecurity to fulfil their responsibilities with regard to the protection of public health. To be effective, regulatory frameworks must establish predictable rules for the tasks of public authorities and foster the meaningful participation of all stakeholders, not just biomedical laboratories. Decision-makers should also bear in mind when embarking on this process that the costs of the implementation of a regulatory framework – to both the regulatory bodies and the laboratories subject to regulation – need to be considered and adjusted to the national economic situation in order to achieve a positive cost–value ratio.

Attention is also drawn to the need for transparency throughout the development and implementation process. There is an onus on national governments to provide information about why and how the national policy for biosafety and biosecurity is developed, how data for the national evaluation and inventory are gathered, and how the core working group and later the NBBC is constituted. Special emphasis should also be placed on the need to engage with the affected public and private stakeholders (e.g. the pharmaceutical and medical device industry, human and animal health professional boards and associations, nongovernmental organizations and the academic sector), as well as the general public, in particular in regard to the development of risk assessment and management strategies for dealing with the public health threats posed by biological risks.

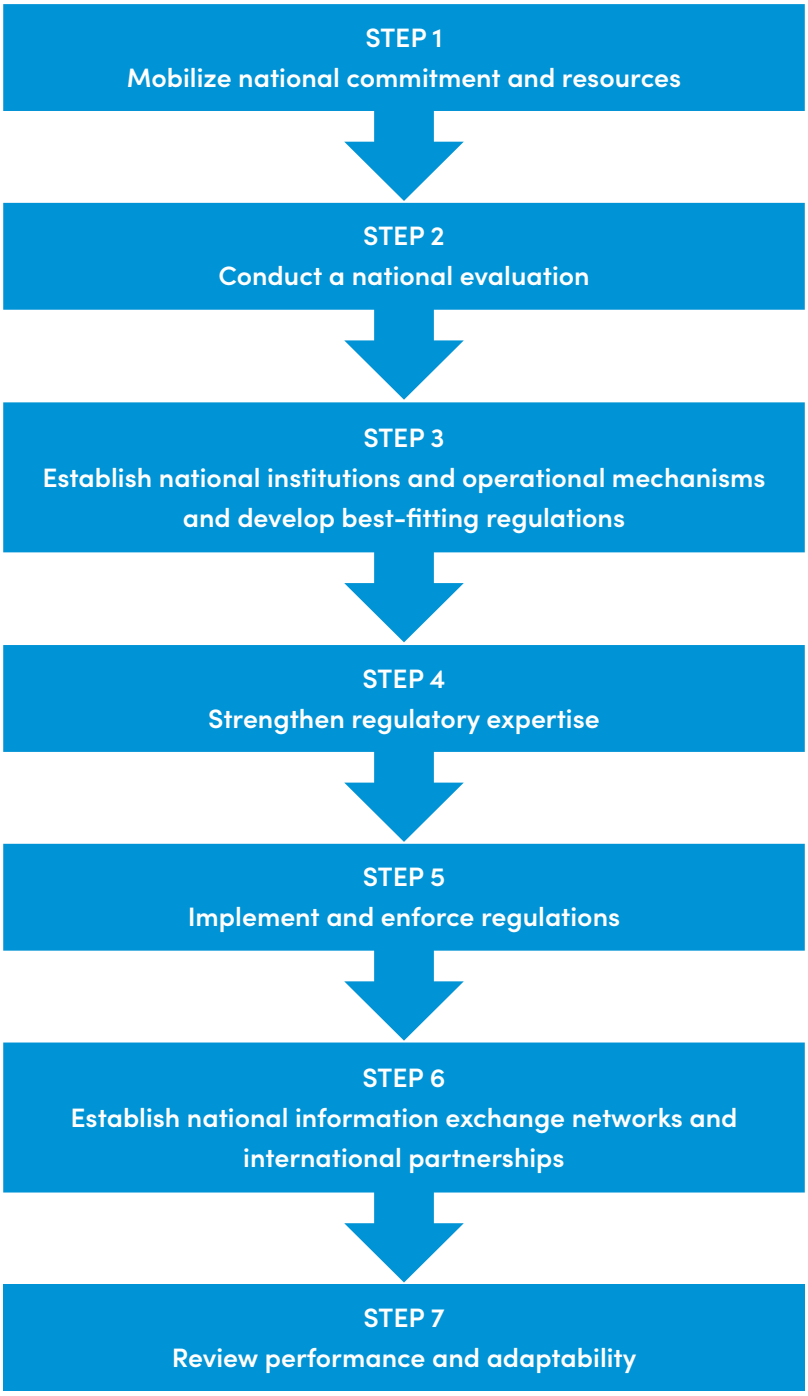

Figure 3.1 Stepwise approach to regulating biomedical laboratory biosafety and biosecurity

3.1 STEP 1
Mobilize national commitment and resources for the development and implementation of a national biosafety and biosecurity policy

High-level political will and commitment are essential prerequisites to the success of any effort to establish a strong national regulatory framework for biosafety and biosecurity. Without the support of national government, any attempt to mobilize resources for developing the work plans and infrastructure needed to formulate and implement a set of regulations governing the activities of biomedical laboratories is likely to meet with considerable resistance.

Given a national commitment to biosafety and biosecurity, the first step in the process is in essence a planning step. The primary objective of this initial step is the development of a national policy on biosafety and biosecurity which sets out the core principles that will inform and guide the subsequent design of the regulatory framework. This policy instrument will serve as an important intentional statement of the government with regard to biosafety and security.

Some of the key decision points and issues which would usually need to be considered as part of STEP 1 of the recommended approach to biosafety and biosecurity regulation are summarized in Table 3.1. Also listed in this table are a number of corresponding policy options; these largely reflect the range of current practice. Additional questions which may help guide thinking and assist users in the conduct of this step may be found in Section C of Annex III (WHO assessment tool: STEP 1).

3.1.1 National commitment to biosafety and biosecurity

Expression of government willingness to engage in matters related to biosafety and biosecurity in and of itself is not sufficient; ideally, the government should demonstrate its commitment by taking a lead role in the development of a national biosafety and biosecurity policy, and equally by allocating adequate resources to this task. However, while strong government commitment is essential, and direct government involvement highly desirable (i.e. as the lead agency), responsibility for developing a national biosafety and biosecurity policy may be shared with other agencies, for example, the national regulatory authority (NRA) (see Table 3.1).

Table 3.1 Selected STEP 1 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS
Is commitment to laboratory biosafety and biosecurity reflected by the presence of a strong governmental lead and the allocation of necessary resources?	While government commitment is essential, engagement in the policy development process may take the form of: • direct involvement (of the national governmental structures) with regard to the design and progression of strategies and action plans • shared responsibilities (with other national regulatory agencies) with regard to the design and progression of strategies and action plans • no direct involvement: design and progression of strategies and action plans specific to biomedical laboratories is undertaken by nongovernmental stakeholders only
Should the biosafety and biosecurity policy be standalone or be incorporated into another relevant national policy?	A national policy may be: • a standalone policy • part of laboratory quality policy • part of occupational health and safety policy • part of heath security policy • part of health policy
How should a national biosafety and biosecurity committee be constituted and set up as part of the biosafety and biosecurity policy?	Membership of the national biosafety and biosecurity committee may be drawn from the following potential stakeholder groups: • regulators (representing the human and animal/environmental health sectors) • laboratory scientists • physicians • national security representatives • (occupational) health organizations • providers of national (health) databases and/or others

3.1.2 National biosafety and biosecurity policies

As indicated above, the purpose of a national biosafety and biosecurity policy is to lay the foundations for the development and subsequent implementation of the regulatory framework governing the activities of biomedical laboratories. Even if laws or regulations relevant to biosafety and/or biosecurity at the laboratory level already exist, countries are still advised to develop an overarching national policy statement as a symbolic anchor in the field of biosafety and biosecurity.

Any national policy for biosafety and biosecurity should be consistent with existing national policies governing laboratory quality, as well as policies that relate to other areas of regulation, such as the food, agriculture, human, animal and environmental health. It may either be developed as a standalone policy or incorporated into another related national policies, strategies or action plans, for example, those dealing with laboratory quality, or occupational health or health security (Table 3.1).

3.1.3 Resources for biosafety and biosecurity policy development: establishment of a national biosafety and biosecurity committee

In most countries, especially those in which national biosafety and biosecurity regulations do not yet exist and/or those with limited regulatory capacity and systems, it is advisable to establish a dedicated national task force or working group to undertake the preparatory work that will be required ahead of developing a national policy. This preparatory work would likely include a preliminary inventory or review of existing legal, scientific and technical in-country structures and capacity in relation to biosafety and biosecurity. Such a review would support the biosafety and biosecurity regulatory system design process and also inform and guide the drafting of an overarching national policy.

Establishment of a working group or task force as part of this first step offers the additional benefit of serving as a forerunner of a more formal national biosafety and biosecurity committee (NBBC). The creation of a NBBC is strongly recommended, with a membership reflecting the interests of all key stakeholders, including regulators, laboratory scientists, physicians, national security representatives, (occupational) health organizations, and providers of national (health) databases (see Table 3.1). It is also advisable to include parties who represent the human and animal/environmental health sectors to ensure the necessary cooperation between these sectors. Most NBBCs, where they exist, are constituted of a mix of both governmental and nongo-vernmental experts.

It is recommended that provision for the establishment of a formal NBBC (if such a body does not yet exist) should be included in the national biosafety and biosecurity policy. Allocation of adequate resources to fund the activities of such a committee should form part of the policy (see Box 3.1). The national policy should also make explicit provision for the creation of effective communication structures between the NBBC and legislative parties and/or national regulatory bodies (e.g. the national regulatory authority).

The wider question of resourcing is one that warrants attention even at this relatively early stage of the process, and should be considered as part of this preliminary step. In addition to identifying resources to support the work of the task force and/or NBBC, it is advisable to also consider the level of resources needed to develop the scientific and regulatory expertise that will be required to undertake the subsequent steps outlined in this document, including in the first instance, STEP 2 (the national evaluation) and STEP 4 (strengthening regulatory expertise). This will ensure that the evaluation of the regulatory environment, as well as any necessary risk assessments, have a scientifically valid basis, and in turn, that government and national regulatory authorities have a balanced and realistic view of the resources required to support the regulatory and laboratory infrastructure at an early stage.

BOX 3.1 NATIONAL BIOSAFETY AND BIOSECURITY COMMITTEES

Countries are strongly advised to create a national biosafety and biosecurity committee (NBBC) or equivalent body to coordinate national efforts to improve biosafety and biosecurity and reduce the risk to public health of exposure to potentially harmful biological agents. In the context of this guidance and the stepwise approach to developing a regulatory framework for biosafety and biosecurity, it is recommended that the NBBC take the lead role in:

- **conducting the national evaluation/situational analysis (see STEP 2)**
- **strengthening in-country regulatory capacity and expertise (see STEP 4)**
- **developing and implementing the regulatory framework and its requirements (see STEP 5)**

In later stages of the implementation process, the NBBC might usefully assume a consultative role and provide the coordinative mechanism needed to periodically assess the scientific, safety, security, ethical and other aspects of the regulatory environment in an independent and impartial manner (see also STEP 7).

3.2 STEP 2
Conduct a national evaluation and surveys

Before substantive work on the design of an effective regulatory system can begin (see STEP 3), it is essential to perform a systematic evaluation of the existing regulatory environment as it relates to biomedical laboratory biosafety and biosecurity. The aim of such an exercise is to characterize the existing in-country regulatory infrastructure and capacity, and to assess the effectiveness of the mechanisms and systems already in place. The results of the evaluation will not only inform evidence-based decision-making and identify regulatory gaps but will also help ensure the efficient use of available resources.

Table 3.2 provides a list of key decision points relating to the possible scope and remit of the national evaluation. Additional signalling questions, designed to assist users carry out this evaluation step, are provided in Section C of Annex III (WHO assessment tool: STEP 2).

It is likely that in order to support the information needs of the systematic evaluation of the exiting regulatory environment, it will be necessary to commission a number of reviews of published data and/or new surveys. Any additional survey work related to the evaluation exercise should be commenced as soon as possible, and ideally be coordinated by the national task force/working group or if such body already exists, the NBBC (see STEP 1).

Results of the analysis and assessment of the information gathered through a combination of reviews and surveys should be synthesized and made available in the form of a written report. The final evaluation report should provide an overview of the following:

- existing human and scientific infrastructure including capacity building programmes (e.g. training programmes for safe use of microorganisms)
- current status of biotechnology and biological agent handling
- existing financial schemes (e.g. for the installation and monitoring of biosafety/biosecurity measures at biomedical laboratories)
- existing reporting system databases
- existing regulatory structures and legislation with regard to biosafety and biosecurity
- existing mechanisms for the development of legislation and "soft law" including administrative and enforcement capacities
- current stakeholders
- prevailing view of the public towards biotechnology, biological agents and their environment
- current mechanisms for regional cooperation and regulatory harmonization (e.g. within economic or regulatory alliances)

Table 3.2 Selected STEP 2 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Is there a need to perform a country evaluation?	If yes, then the following questions need to be answered: • Who will perform it? • What is the timeframe? • How will the evaluation be performed? • What is the anticipated outcome? • What are the resources required?

Table 3.2 Selected STEP 2 decision points and policy options (continued)

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Which key elements of the regulatory environment relating to biosafety and biosecurity does the evaluation need to describe and assess?	A comprehensive evaluation is likely to cover most if not all of the following: • The characteristics of existing regulatory frameworks in terms of: → scope → advantages → constraints → adaptability → status → empowerment → hierarchy/structure • Existing mechanisms for the development of public policies, regulations and legislation • Infrastructure, to include both: → human resources (scientific, administrative, enforcement) → financial resources • Stakeholders • Current status of biomedical laboratories, detailing for instance: → number of laboratories (by category, e.g. research, teaching, production, diagnostic) → type of pathogens handled → type of activities carried out → type and status of research → list of pathogens (including security-sensitive biological agents) → current programmes for safe handling of microorganisms • Participation in International treaties, agreements and protocols • Existing capacity building programmes • Existing mechanisms for regional and/or international cooperation and harmonization • Breadth and availability of biosafety and biosecurity related data (e.g. from reporting systems databases, published reports)

Although it might not be possible to report on all of the above elements at the same time, the evaluation report should at the very least provide an impartial overview of the national situation with regard to the management of biosafety and biosecurity at biomedical laboratories. For the purpose of characterization of the country´s situation, it is recommended (in the interests of avoiding sampling bias) that the evaluation target public laboratories and facilities in the case of services (e.g. diagnostic laboratories) where the private sector and/or nongovernmental organizations (NGOs) also play a role.

It may be instructive to include a review of the approaches to biosafety and biosecurity regulation adopted by other countries as part of the evaluation; this may not only provide useful learnings and points of comparison but also justification for the direction national-level policy development might ultimately take. Furthermore, taking account of the experience of other countries might help to identify an appropriate regulatory model that could be adopted, as is or with modification, as well as widen the evidence base for proven regulatory policies, strategies and procedures. For this purpose, the responsible governmental or regulatory bodies should consider establishing relationships with other national regulatory agencies and/or international institutions that can offer additional advice and guidance (see STEP 6). Membership of international networks offers additional benefits, most notably in terms of support for identifying and managing new and emerging infectious agents, and help with other challenges, for example, quantifying and managing risks associated with new technologies (see also STEP 6).

3.3 STEP 3
Establish national institutions and operational mechanisms and develop best-fitting regulations

Once the general principles have been agreed and enshrined in government policy (as part of STEP 1), it will then be possible to establish the necessary institutions and mechanisms that will underpin the development and subsequent implementation of a comprehensive national biosafety and biosecurity regulatory framework (NBBF). Much of the information needed to inform and guide this key step will have been gathered as part of STEP 2, the evaluation step, described previously (see Section 3.2).

While the overarching goal of this key third step is the realization of an efficient, integrated regulatory system for managing biological risk at the national level, for convenience this step may be divided into a series of discrete tasks or sub-steps. In practice, however, it is likely that these tasks would be conducted in parallel. The key tasks that together constitute STEP 3 of the recommended approach to establishing a national regulatory framework for biosafety and biosecurity may be summarized as follows:

- ensure that all existing institutions or organizations involved in matters related to biosafety and biosecurity have been identified and that their regulatory roles and responsibilities have been fully described and understood
- identify which regulatory bodies have responsibilities for each of a number of predefined areas of activity (this could be thought of and treated as a "mapping" exercise)
- formulate an overarching, integrated framework for managing biological risk at the national level, taking into account any identified gaps and overlaps in the existing regulatory system
- decide what additional administrative structures would be needed to best develop and implement this framework
- develop a set of fit-for-purpose regulations and requirements in line with the new NBBF (this may involve amending existing regulations or introducing new regulations)
- pilot the proposed regulations as part of a stakeholder consultation process

Some of the main STEP 3 decision points, with corresponding policy options and/or additional issues that may need to be considered, are listed in Table 3.3.

Table 3.3 Selected STEP 3 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Institutional arrangements	
What kind of administrative structure is best suited to the national situation and circumstances?	Options include: • a single department or entity in charge • a distributed authority/distributed responsibility
Development of the framework and best-fitting regulations	
Does the country want/need new legislation?	Options include: • use existing legislation • amend existing legislation • draft new legislation

Table 3.3 Selected STEP 3 decision points and policy options (continued)

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
If new legislation is required, what should it cover?	Options include: • in terms of "products" – human pathogens, animal pathogens, genetically-modified organisms, all microorganisms or security-sensitive biological agents • in terms of "processes" – handling of pathogens, import and export, and/or research • a mix of both products and processes
How will the various elements and aspects of biosafety and biosecurity be covered by rules and regulations?	Options include: • all aspects covered under a single new act/regulation • different aspects covered by different/separate acts/regulations
What elements and aspects of biosafety and biosecurity should be covered by the proposed framework?	Potential items for inclusion include: • scope • definitions • competent authority and advisory committee and their responsibilities • biosafety and biosecurity programme at institute level • responsibilities at institutional level • risk assessment • packaging and transport • good microbiological practice and procedures • licence/authorization requirements • waste management • training • accident/Incident reporting • practitioner/laboratorian level topics • guidelines • decontamination • spill clean-up • Information exchange/ capacity building • Inspections/audits • documentation and record keeping

Table 3.3 Selected STEP 3 decision points and policy options (continued)

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Does the proposed regulatory framework follow the "One-Health" approach?	• In terms of legislation, options include: → single act/regulation which covers both human and animal pathogens as well as environmental issues (where applicable) → different acts/regulations cover human and animal pathogens as well as environmental issues separately, where applicable • In terms of institutional arrangements, possible options include: → single authority in charge of both human and animal pathogens → separate authority in charge for human and animal pathogens
How should the public be involved in the development of the national regulatory framework?	The main options are : • public consultation • public notification
Should the proposed framework allow for subsequent amendment (or reform) to take account of changes in technology and/or to incorporate other changes as deemed necessary?	The main options are: • allow a fixed time period after which a review should be carried out • stipulate mechanisms which initiate/trigger amendments or reforms to the regulations Additional issues to be considered include: • delineation of responsibilities for the review/reform process • whether these responsibilities should be determined by the type of trigger

3.3.1 Institutional arrangements

A key task to be undertaken as part of STEP 3 follows directly on from STEP 2. An evaluation conducted according to STEP 2 of this recommended approach should have provided the information necessary for understanding the distribution of regulatory responsibilities, that is to say, which institutions have responsibility for which aspects of regulatory control with regard to the activities of biomedical laboratories.

Given this understanding, and in order to inform the design of an overarching regulatory system for managing biological risk at the national level, users of this guidance are encouraged to perform a mapping exercise, the purpose of which is to identify which regulatory bodies have responsibilities for each of the following key areas of activity:

- legislation
- compliance and enforcement
- surveillance, monitoring and reporting
- inspection services
- diagnostic services
- emergency response to incidents (e.g. disease outbreaks or major spills)
- scientific research and advice

As a result of this mapping task, it should be possible to identify any gaps in the exercise of these seven core regulatory functions and responsibilities, and whether any de facto arrangements exist by which existing institutions correct any overlaps or gaps. It should also be possible to identify overlaps and potential conflicts in the current legislation governing the activities at biomedical laboratories. Armed with the insight gained by conducting such an exercise, it should then be possible to devise an efficient, integrated system of regulation for managing the totality of biological risk.

In countries where several regulatory bodies already exist, the identification of gaps and overlaps in the regulatory environment is especially important. Where overlaps are identified, consideration will need to be given to how best to promote coordination among the agencies with overlapping and potentially conflicting responsibilities for regulating biosafety and biosecurity. It may even be necessary to redistribute the technical and human resources of existing regulatory agencies to rationalize the extent and characteristics of their functions in the interests of creating a NBBF that is both comprehensive and efficient.

In terms of the institutional structures and arrangements needed to fully integrate the functions and responsibilities of existing regulatory bodies and to rationalize the regulatory framework as it relates to biosafety and biosecurity, most decision-makers are presented with two main options:

- Option A: to create a new regulatory body at a supra-ministerial level
- Option B: to use existing legal and institutional structures while establishing a coordinating mechanism to exercise an oversight role

While option A – the creation of a new regulatory agency with "end-to-end" functions and responsibilities – offers a number of advantages (e. g. high governmental and public attention, effective use of resources, prevention of loss of information through the use of optimized information channels), it may not be viable or practicable for some countries on the grounds of cost and/or an unfavourable political climate.

The alternative – option B – means that the regulation of different aspects of biosafety and biosecurity will continue to be regulated by different sectors. For example, the transport of infectious substances would remain under the jurisdiction of the department of transportation, the use of genetically-modified organisms (GMOs) and animal health would be regulated by the agricultural sector and the food safety agencies, and the containment of high-risk organisms would be controlled by the security sector. This option would require the installation of a coordination mechanism to monitor the existing regulatory agencies and will necessitate the acceptance of existing regulatory bodies to such oversight and shared arrangements. The coordinating mechanism would need to be institutionalized by an appropriate council or committee (such as the NBBC) and empowered by law.

Whichever option is chosen as the basis for the organization and allocation of regulatory responsibility within an overarching regulatory system, involvement of the national regulatory authority (NRA) in the decision-making process is strongly recommended (see Box 3.2).

BOX 3.2 NATIONAL REGULATORY AUTHORITIES

The vast majority of countries have a public-service national regulatory authority or NRA to ensure that all pharmaceuticals and biological products (e.g. vaccines, live viruses, genetically-modified organisms) used within a country are safe, effective and of good quality, that is to say, meet national and international standards of quality and safety.

In most countries, the NRA is the enabler of primary and secondary legislation. In the context of this guidance, it is envisaged that the role of the NRA – in addition to ensuring that any new laws and regulations are implemented and enforced –,is one of an independent and impartial decision-making stakeholder in the process leading to the development and implementation of the NBBF.

In addition, the NRA is well placed to provide, through periodic reporting on its activities, an impartial and balanced review of the effectiveness and efficiency of the new or revised regulatory framework it is in place (see also STEP 7).

3.3.2 Development of best-fitting regulations

Having established, at least in outline, how the responsibilities for regulatory oversight of biomedical laboratories might be distributed among the respective administrative structures and bodies, the next key task is the development a set of best-fitting regulations for biosafety and biosecurity.

Table 3.4 explores some of the options available to decision-makers tasked with developing an integrated regulatory system for laboratory biosafety and biosecurity. Note that this list – again based on a review of current practice – is by no means exhaustive, but merely serves to highlight what are likely to be the most relevant

elements and areas of regulatory control that will need to be considered. It is acknowledged that country situations differ and that the selection of a particular policy option or strategy over another will depend on national or regional contexts and on other pertinent factors such as existing regulatory structures and legislation.

A key consideration, and one that is now widely believed to be central to the management of biological safety and more specifically to the development of national biosafety and biosecurity regulations, is the role of local risk assessment[2]. Over the past decade or so, biological risk management strategies have evolved in tandem with advances in available technologies. There is now a growing consensus in favour of more flexible, risk- and evidence-based approach to biological risk management at the laboratory level, one that reduces the traditional focus on pathogen risk groups and biosafety levels in favour of a greater emphasis on human factors and worker training *(2, 3)*. By basing the selection of all risk-mitigation measures on the results of a thorough and multifactorial risk assessment, one which also takes into account wider laboratory-specific factors that impact on risk levels such as volume or titre of biological materials being handled, worker competency, transmission routes and prophylaxis availability, the evidence-based risk assessment approach ensures that laboratory facilities, safety equipment and work practices, are more locally relevant, proportionate and sustainable *(3)*.

In countries with regulatory systems for biosafety and biosecurity already in place, regulations tend to be based on the more conventional approach to hazard assessment, whereby risk mitigation and containment measures are selected (and mandated) according to the pathogen categorization or risk group. Pathogen risk groups also tend to form the basis of many existing notification or authorization processes and regulations. While risk groups can be a useful basis for national regulatory systems, applying them universally does not take into account the above-mentioned range of individual laboratory factors. This means that opportunities to develop regulatory controls that are proportionate to the assessed risks may be missed *(3)*.

When developing a new (or revised) regulatory framework for biosafety and biosecurity, users of this guidance are thus urged to place strong emphasis on locally-conducted risk assessments and develop regulatory requirements which are based on appropriate risk criteria and reflect considerations such as good microbiological practice and procedures, standard operating procedures (SOPs) and worker training. The regulatory framework should also take into consideration all types of risk assessment – namely for pathogens, organizations, facilities and operating procedures. Users are also advised to ensure that sufficient resources – guidance documents, biosafety and biosecurity evidence data, scientific support – are made available for carrying out appropriate risk assessments. Particular emphasis should be placed on human resources and the level of competence required to conduct the necessary local risk assessments (see also STEP 4). Additionally, a mechanism should be put in place which allows individual facilities to communicate with the appropriate regulatory body or bodies and conversely, allows regulatory authorities to evaluate local risk assessments.

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[2] Risk assessment in the context of this guidance document may be described as a systematic process for gathering and evaluating information to support the development of regulatory requirements that are risk- and evidence- based.

Countries that already have or are considering national oversight mechanisms for biosafety and biosecurity but have yet to develop their local risk assessment capacity are advised to adopt a flexible approach to NBBF development; this will allow for multiple solutions and mitigation methods. For instance, if risk groups and biosafety levels have already been developed at the national level and are embedded into legal frameworks, then provision should be made for periodic reviews of those risk groups such that any new evidence which supports a change in the risk profile of a given pathogen can easily be incorporated. National frameworks should also factor in review mechanisms which ensure that the safety procedures being conducted at individual laboratories are appropriate, i.e. sufficient to control the risk(s) identified.

Table 3.4 Developing a comprehensive regulatory framework for laboratory biosafety and biosecurity: Selected issues to consider and examples of current practice as a guide to possible policy options

ELEMENT	OPTION 1	OPTION 2
Scope	Covers all microorganisms	Emphasis on genetically-modified organisms and/or security sensitive biological agents
Approach to risk assessment	Uses an evidence- and risk-based approach Flexible approach whereby local and national risk assessment is performed by adequately trained experts and monitored for appropriateness by national regulatory mechanisms	Uses a compliance-based approach Inflexible risk determination based on super-regional standards that are not necessarily (fully) applicable to the local/individual circumstances
Competent authority and its responsibility	Single regulatory authority in charge	Multiple regulatory authorities in charge
Registration and licensing procedures	Adequate requirements for the authorization process, training, reporting, documentation etc.	Inadequate requirements for the authorization process training, reporting, documentation etc.
Flexibility	Regulations are updated/revised incorporating changes (state of the art technology)	Regulations are not updated/revised

Table 3.4 Developing a comprehensive regulatory framework for laboratory biosafety and biosecurity: Selected issues to consider and examples of current practice as a guide to possible policy options (continued)

ELEMENT	OPTION 1	OPTION 2
Documentation and record-keeping	Guidance documents and standards available to aid implementation	No guidance documents and standards available on time
Information exchange	A mechanism for regional cooperation and harmonization	Multiple levels of bureaucracy due to multiple pieces of regulations and/or multiple regulatory bodies
Integration with the "One health" approach	One-Health approach taken by the framework	No cohesive approach between the human and animal sectors
Information exchange	International cooperation and exchange	Limited view on purely national concerns

The remainder of this section briefly reviews some of main areas of biomedical laboratory activity that regulations will need to address within the context of a comprehensive and overarching NBBF. In each case, factors which may influence the choice of regulatory approach are briefly reviewed in order to assist users develop a set of best-fitting regulations that are apposite to their own country circumstances.

Registration and authorization procedures

Ensuring that facilities which handle biological agents do so in such a way to protect both their workers and the public at large from undue exposures to biological agents – by adopting appropriate safety measures – is an important part of effective regulatory control and overall risk management. To this end, many countries have established registration and authorization systems in order to track and monitor the activities of individual biomedical laboratories.

Typically, such systems specify which activities involving biological agents – for example, possessing and inventory, handling, modifying, and importing/exporting – require a permit or a licence, or some other form of authorization before they can be undertaken. Many existing national frameworks prohibit the handling and processing of high-risk and security-sensitive biological agents unless a valid licence or permit is obtained.

To promote efficient functioning of a licensing system within an overarching NBBF, it is important to identify and define the responsibilities of the regulatory authority/ authorities in charge of registration and licensing. Procedures for submitting application documents, as well as any criteria for exemption from licensing, notification obligations, conditions for revocation, and requirements for certification, should also be clearly specified. Although the amount of information requested by the licensing body as part of an application for a licence or authorization to handle a biological agent will vary according to the risk profile of the facility, it is generally recommended that an application should, at a minimum, require specification of:

- the aim and objectives of the proposed controlled activity
- the name of the biological material
- type of controlled activity proposed
- details of the facility/laboratory
- local risk assessment report
- the proposed risk mitigation measures

When drawing up an efficient system of registration and authorization as part of a NBBF, regulators are advised to give some thought to competing demands of the need for detailed information and overly burdensome application systems. Attempts should be made to streamline the application process as far as is practicable by avoiding unnecessary and overly-demanding paperwork but without compromising safety.

For the licensing purposes, some countries may decide to classify the biological agents into risk groups based on each biological agent's characteristics, its epidemiological profile and the likelihood it will cause and spread infection in humans or animals in the country, and the consequences to individuals and public health if infection were to occur. In this case, and as discussed above in the context of risk assessment, it is recommended that the NBBF include a mechanism which allows the list of classifications of biological agents to be periodically updated and newly-emerging biological agents to be added to this list.

Incident reporting

In addition to licensing and authorization systems, NBBFs should also establish the basis for reporting incidents, that is, any non-routine exposure(s) to biological agents within a facility. By recording all incidents that occur at the facility level (and at the national level), systems for incident reporting can play a vital role in risk mitigation. A proper investigation of incidents according to their severity and consequences will ensure identification of the cause and help develop, implement and monitor plans to mitigate against future incidents of a similar nature.

It generally recommended that incident reporting systems should be set up to record any incidents that involve exposures to biological agents, either accidental or

intentional; special provision may be warranted for reporting the loss, theft or misuse of security sensitive biological agents (SSBAs). The incident reporting system should also cover the medical surveillance of illnesses and absenteeism among the workforce that might be associated with their laboratory duties and responsibilities.
Careful consideration should be given to the reporting mechanisms and lines of communication, as well as the related responsibilities of laboratory personnel with regards to the reporting of incidents; these should be clearly defined as part of the NBBF. Above all, the system should encourage laboratory personnel to report incidents, for example, by adopting methods for anonymous reporting. In this regard, the role of local leadership cannot be overemphasized in forging and maintaining safety culture and an atmosphere where safety is valued and prioritized, and there is a real commitment to safety at all levels within an organization.

In terms of regulatory requirements, it is common practice to specify which incidents require reporting, the internal and external reporting process to be adopted, the reporting timelines, the institutional-level responsibilities and the minimum amount of information to be included in any incident report. For instance, the minimum reporting requirements might include:

- information regarding the institution
- nature of the activity
- nature of the incident
- biological material involved
- emergency response
- measures taken to preclude its reoccurrence

Incident reporting systems are a valuable resource, providing biosafety and biosecurity evidence data which can be used to assess and evaluate the effectiveness of safety measures.

Transportation of biological materials

Biological agents, as well as blood and tissue samples and waste materials containing pathogens, are routinely transported for a wide variety of reasons, both within facilities and countries and across international borders. The potential for accidental releases of pathogens and personnel exposures during transportation means that regulatory frameworks should include requirements which ensure the preservation of the integrity of biological materials and infectious substances during this time.

The primary aim of regulatory control of the transportation process is to ensure that any change in possession of biological agents is in the best interests of the involved people and is accomplished with a high regard to public health. The regulatory framework should therefore require both a justification of the need to transport the biological material and a subsequent approval of the transportation process by an appointed regulatory authority.

The NBBF should address the full range of potential transportation routes, including from facility to facility in the same or a different country, between laboratories on different sites within the same facility, and between laboratories within the same building. In addition, all activities relating to the transport of biological materials should be covered by some form of regulatory control; these activities range from planning/scheduling (of the transportation), risk estimation, packaging, labelling, documentation, training, through to spill clean-up and incident reporting. A regulatory environment which places an emphasis on establishing a good working relationship between the sender, the carrier and the receiver will help to ensure that biological materials and infectious substances are transported in a as safe and timely manner as possible.

Various international regulations and recommendations relating to the transport of dangerous goods including infectious substances exist and which may be used as a basis for drafting or revising national and sectoral regulations relating to transportation within the context of the NBBF. The United Nations (UN) Model regulations on the transport of dangerous goods *(14)* is particularly comprehensive in that it covers the regulation of the transport of infectious substances by all modes of transport. These recommendations are the remit of the United Nations Economic and Social Council's Committee of Experts on the Transport of Dangerous Goods (UNCETDG).

The broad principles governing the international transport of dangerous goods by air are contained in Annex 18 to the Chicago Convention on International Civil Aviation – The Safe Transport of Dangerous Goods by Air *(15)*. Technical instructions for the safe transport of dangerous goods by air, produced by the International Civil Aviation Organization (ICAO), provides the technical information in support of the safe international transport of dangerous goods by air. Although aimed at governments and the international organizations responsible for ensuring safe transportation of dangerous goods, their recommendations are not legally binding. However, they are structured in such a way that they could be directly transferred into national and sectoral regulations, while also providing the flexibility to accommodate any special requirements. A WHO guidance document on regulations for the transport of infectious substances provides additional practical advice on how to achieve compliance with the above-mentioned international regulations and recommendations *(16)*.

Biosafety programme management

Good laboratory practice dictates that any facility or institution that handles biological agents should have in place a biosafety management programme, that is to say, a set of policies and structures for managing the totality of risks to biosafety at the institutional level. Biosafety management programmes ensure that facilities adopt and comply with safe and secure microbiological practices and procedures, and that these practices and procedures in accordance with national and international regulations and guidelines.

Many laboratories have made use of the laboratory biological risk management standard CWA 15793 (expired in 2014) *(12)* as a basis for their biosafety management programmes. Given its popularity, the new ISO standard, ISO 35001 Biorisk Management for Laboratories and other Related Organizations, incorporates many of the older CWA standard's principles (see also Section 2).
In order to be effective, biosafety management programmes need to integrate several key risk management functions, providing not only a comprehensive safety policy, secure laboratory facilities and operational safety equipment but also regular staff education and training programmes in order to foster a facility-wide culture of safety. It is equally important that national regulatory frameworks adopt a similarly integrated approach to managing the risks associated with biological materials in order to ensure adequate protection of public health. This means that NBBFs should incorporate requirements covering the full spectrum of biomedical laboratory activity including management structures, roles and responsibilities, monitoring and evaluation functions, and staff training, as well as the need for continual improvement of safety policies and processes. To ensure a fully integrated and comprehensive approach to risk management at the institutional level, some countries have mandated the formation of an oversight committee and the designation of individuals to oversee the totality of a facility's biosafety (and also biosecurity) practices *(17)*.

Monitoring and surveillance

As is the case with any regulatory system, it will be important to ensure effective implementation of, and compliance with, the NBBF and all its component requirements. Specifications of the NBBF will therefore need to include mechanisms for compliance monitoring and surveillance; this aspect of the framework should identify the regulatory authorities and/or organization that will be tasked with conducting compliance monitoring and surveillance. The remit and responsibilities of these agencies in terms of compliance monitoring and surveillance should also be clearly defined in the NBBF. It should be further noted that there needs to be effective coordination between the systems for authorization and incident reporting and surveillance in order to ensure proper functioning of the overall regulatory framework.

Different approaches can be taken to monitor compliance. The results of the national evaluation conducted as part of STEP 2 should help to inform decisions about the most appropriate approach to adopt, given country circumstances and existing regulatory infrastructure (see also STEP 2). Some countries have opted to establish a national body, often a committee such as the NBBC, to administer the monitoring and surveillance element of the regulatory framework. A NBBC (or equivalent body) may have several responsibilities, such as drafting codes of practice, providing advice and recommendations to the regulatory agencies responsible for surveillance, and undertaking or commissioning research, as well as creating awareness for monitoring activities (see also Box 3.1). It is critical that such a body is comprised of experienced practitioners who have an in-depth understanding of the technical aspects of processes being monitored, or in the event that such expertise does not exist within its membership, the means and resources to call upon the advice of external experts as appropriate.

With regard to the monitoring and surveillance of regulatory compliance, good communication between all stakeholders is key. While laboratory managers need to be aware of any regulatory conditions that impact their work (and comply with them), it is equally important that those tasked with developing national frameworks and oversight mechanisms understand the implications of the framework at the laboratory level. As in other areas of regulatory activity – there is a need to strike a collaborative balance between voluntary, independent peer review by stakeholders (e.g. health professionals' audit systems, governance and certification/accreditation systems) and statutory, governmental control (e.g. licensing, registration and inspection) in the interests of developing an overarching system of appropriate and proportionate controls and a safety culture that is built on a national commitment to biosafety *(17).*

Laboratory biosecurity

In the interests of national and indeed international biosecurity, it is vital that a NBBF comprises elements which regulate the possession, use and access to biological materials. The primary objective of such measures is to prevent biomedical laboratories from becoming the sources of unauthorized possession of potentially harmful biological agents, which could lead to the intentional release or the malicious use of pathogens to commit acts of bioterrorism.

In countries with established regulatory systems for biosecurity, regulations generally take the form of laws that require individual laboratories to apply for licences and/or security clearance to handle, store or move biological materials that are deemed to be "security sensitive". While specification of security sensitive biological materials may well underpin regulations aimed at controlling materials that constitute a threat to national biosecurity, regulators are encouraged to widen their remit, and to also consider developing requirements (paralleling the situation for biosafety) that relate to the management of laboratory biosecurity in its entirety. Important components of biosecurity management programmes include training and inventory/information management, as well as procedures for ensuring transport security, all of which should be included in the NBBF.

Regulatory responsibility for biosecurity should be defined in the NBBF. This may be shared among several regulatory authorities, but, in common with the recommendations made above with regard to biosafety, respective roles and responsibilities need to be clearly delineated.

Given that effective biosafety practices are the foundation of laboratory biosecurity, this guidance also recommends adopting an integrated approach to regulating laboratory biosafety and biosecurity. However, it is acknowledged achieving fully integrated legislation may be problematic and that many countries already regulate laboratory biosafety and biosecurity separately. Only in rare cases are biosafety and biosecurity covered under the same legislation (see Annex II).

Research laboratories, especially those engaged in dual-use research of concern (DURC), represent a particular regulatory challenge. The recommended approach is one which allows a degree of laboratory and medical–scientific self-governance while providing the necessary protection and oversight through regulations which prevent the misuse of dual-use research and other laboratory activities. This approach relies on there being an enhanced culture of trust, personal responsibility, accountability and transparency in laboratories, a culture which comes from strong leadership and a commitment to championing ethics in the workplace. This may be reinforced by a system of sanctions or punishment in the event of offences against regulations pertaining to dual-use research in order to reduce the risk posed by research that can be used to do harm.

It is recommended that the NBBF promote regular and comprehensive assessment of the dual-use potential of laboratory activities. This recommendation is driven by the recognition of the rapid advances in modern technology (e.g. the de novo synthesis of certain viruses), especially with regard to the recurrence and fast expansion of pathogens that were thought to be successfully combatted. Periodic trainings that emphasize risk-based safety and dual-use research potential should be recommended for all stakeholders, including scientists, academics and regulatory officers in order to increase awareness and understanding of new and emerging threats to biosafety and biosecurity.

While this guidance promotes an emphasis on local risk assessment as the basis for selecting nationally-appropriate control measures (see above), when considering the biosecurity elements of a NBBF, there are several international instruments that should also be consulted. The proliferation of biological agents is addressed by The United Nations Security Council Resolution 1540 *(9)*, the Biological Weapons Convention *(8)* and The Australia Group *(18)*, and should be taken into consideration while developing or revising regulations aimed at preventing the undesired release of pathogens through unauthorized synthesis or possession. WHO's Laboratory biosecurity guidance *(19)* addresses basic principles and best practices relating to laboratory biosecurity. Member States are encouraged to include these concepts into their local contexts and frameworks.

Waste management

The safe decontamination and disposal of laboratory waste, being a potential reservoir of pathogens, represents a further important area of activity that should be addressed by any regulatory framework. Countries have approached the regulation of waste processing in a number of different ways. Some have included regulatory controls on the decontamination and management of medical wastes as part of their primary or secondary legislation pertaining to laboratory biosafety or biosecurity. Others have chosen to regulate the management of medical wastes using environmental or other sectoral regulations.

Whichever approach is adopted, it is important that the entire waste management chain is adequately regulated and monitored. This means putting in place regulations which ensure institutional responsibility for not only the safe disposal of different categories of wastes but also their safe collection, segregation, decontamination, packaging, storage and transportation. For example, some types of waste might require processing by autoclave, or some other approved decontamination technology, to achieve satisfactory levels of biological safety prior to disposal. Others may need to be packaged and transported in appropriate containers for decontamination and/or safe disposal at a different facility.
In keeping with the recommended emphasis on local risk assessment as a basis for the selection of mitigation measures, the NBBF should incorporate documentation and technical information pertaining to appropriate decontamination techniques and other relevant waste management processes. The framework should also consider the level of human and technical resources that are required to perform the waste management functions effectively, and make provision for worker training as necessary (see also STEP 4).

Cooperation within the "One Health" concept

When developing or updating a national regulatory framework, decision-makers are advised to pay particular attention to the concept of "One Health", a global concept which aims to address health risks at the interface of human–animal ecosystems *(20)*.

In keeping with the One Health concept, NBBF should promote a comprehensive and integrated approach to risk management across the increasingly interlinked human and animal health sectors, as well as the overlapping aspects of human health, plant health and food safety. The regulatory framework should strive to streamline risk management practices across the human and animal health sectors while enabling individual regulatory authorities to administer their competencies and responsibilities unambiguously.

In terms of creating a NBBF that is aligned with the One Health objectives and supports government efforts to improve collaboration between the human and animal health sectors, the following three areas of activity are considered key targets for regulation:

- surveillance and information sharing
- coordinated response
- biological risk reduction

It is recommended that the development of intersectoral coordination mechanisms in these three areas, which could be facilitated by the NBBC or a similar such body, be incorporated into the regulatory framework.

3.3.3 Stakeholder involvement

Before implementing the new NBBF (see STEP 5), it is advisable to test the application of new regulations and guidelines in selected settings during a period of stakeholder consultation. This consultation phase will promote confidence in the elements of the framework and will increase the overall transparency of the subsequent implementation process. Assuming a positive response to an evaluation of the stakeholder consultation, nationwide implementation of the regulatory framework can then proceed, taking on board any lessons learned as appropriate. Key stakeholders will likely include representatives of various professional organizations and expert committees, as well as biomedical laboratory staff whose work practices will be subject to the new or revised regulations.
Mechanisms for involving key stakeholders in the consultation process include the following:

- **Advisory committees:** The opinions of advisory committees, particularly those tasked with evaluating the scientific, economic, technical and ethical and dimensions of biosafety and biosecurity will provide valuable feedback regarding the feasibility of implementing the new NBBF as intended. Ideally, committee membership should include one or more members of the public.
- **Individual stakeholder group meetings and consultations:** Meetings with individual stakeholders which include feedback mechanisms provide a good opportunity for competent authorities to listen to the views of various stakeholder groups. It should be noted that the general public represents an important stakeholder group; meetings and consultations involving the public should ideally include public education and awareness-raising of issues related to biosafety and biosecurity.
- **Pilot studies:** Pilot studies can provide useful information and feedback relatin to the implementation process; pilot studies should be evaluated and the findings published in the form of a written report.

Open communication and dissemination of the outputs of the above activities will help improve acceptability, transparency and public accountability of the NBBF, and help ensure that its requirements are valid and founded on sound evidence.

3.4 STEP 4
Strengthen expertise to support implementation of a suitable regulatory system

The technical knowledge and skill base of a country represents a key resource and one on which successful development and implementation of a regulatory system for biosafety and biosecurity depends. The continual development and strengthening of core competencies thus represent a key step in the process of implementing effective biosafety and biosecurity regulations. Particular emphasis needs to be placed on building expertise in the safe and secure handling of biological agents in order to increase scientific capabilities in the key areas of evidence-based risk management, inspection and monitoring, all of which are central to a well-functioning NBBF.

Once existing regulatory structures and in-county capacity for handling biological agents have been understood and characterized (as part of the evaluation conducted in STEP 2), a similar exercise to that recommended at the start of STEP 3 may be conducted in order to identify current gaps in scientific and regulatory expertise. Steps may then be taken to build capacity in those areas, as appropriate. Building technical, scientific and regulatory capacity in this way will in turn help to further develop the content and the effectiveness of the NBBF in the longer term.

STEP 4 of the stepwise approach is thus primarily concerned with assessing and building the scientific and technical capacities needed to support the implementation of the NBBF. Pertinent decision points, together with selected policy options are listed in Table 3.5. A number of additional issues that may need to be taken into consideration during this capacity building step are also included where appropriate.

Appropriate education and training programmes will be important tools for building the scientifically sound knowledge and technical expertise needed to support the development of an effective regulatory framework. To this end, training programmes should be developed to meet the specific needs of the national regulatory framework. In particular, consideration should be given to strategies that will best deliver the ongoing need for trained individuals who will likely form the pool of experts responsible for directing the future development of the NBBF, especially in the context of the risk assessment and management related activities.

Table 3.5 Selected STEP 4 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
What is the best way to incorporate scientific advice into the decision-making process?	Possible options include: • set up an independent expert/scientific advisory committee • develop competencies in government departments and agencies • rely on a combination of both of the above
Does all of the necessary expertise reside in-country, or is there a need to supplement this by calling on external experts and/or developing new training programmes to meet the needs of the NBBF?	In terms of developing the necessary regulatory expertise, possible options include: • use international experts and/or external reviews • build domestic self-sufficiency and capability through training • rely on a combination of both of the above There is also a need to consider how best to develop national capacity and expertise in scientific risk assessment, and how this might be coordinated at the national, regional and subregional level.
Resources and mechanisms for strengthening regulatory expertise	When reviewing options for strengthening regulatory expertise, additional issues to consider might include: • What is the current scenario of expertise within the national regulatory authority? • Are there adequate foresight mechanisms within government departments in place to identify potential knowledge gaps, and are there existing avenues to access training or the recruitment of state-of-the-art knowledge? • How might the scientific advisory committee be involved in developing best-fitting regulations (e.g. amending regulations in light of advances in technology, evaluating risk assessments, advising on specific issues of uncertainty)? • Is a mechanism in place by which the national regulatory authority can monitor the appropriateness of the risk assessment process and its outcomes?

Table 3.5 Selected STEP 4 decision points and policy options (continued)

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Location and roles of the scientific advisory committee and experts involved in risk assessment and related functions	In terms of the development and institutional organization of risk assessment expertise, possible strategies include: • reliance on local (i.e. facility-level) risk assessment with periodic monitoring and oversight evaluation by governmental departments • development of core competencies for risk assessment within government departments and agencies • reliance on expert advisory committees (as opposed to a reliance on a combination of in-house and external scientific expertise) In terms of apportioning responsibility for risk assessment monitoring and evaluation functions, possible strategies include: • concentrating the risk assessment monitoring functions within a single identifiable body (e.g. a gene technology regulator) • distributing the risk assessment monitoring functions among different government departments and ministries (e.g. department of health, department of animal health)
Collection and use of applied biosafety and biosecurity data	Important considerations are: • What kind of data should be collected? • What arrangements need to be put in place to facilitate international exchange of data?

When planning national training programmes, users of this guidance may find it constructive consider and address the following questions (see also Table 3.6):

- Should the country rely on international experts or is domestic self-sufficiency and capability an appropriate goal in a mid-term or long-term perspective?
- What is the best way to develop and manage core competencies for risk assessment?
- How can scientific and technological advances (e.g. with regard to techniques for GMO detection and monitoring) be incorporated into the evidence-based risk assessment process?
- Will it be possible to develop sufficient knowledge and expertise within governmental departments/agencies to support risk assessment activities and programmes, or will it be necessary to rely on the NBBC and/or additional expert

advisory committees or a combination of both (i.e. "in-house" and external scientific expertise) in order to fulfil this function adequately?

- Should the risk assessment function be concentrated within a single identifiable body or be distributed among different governmental departments/agencies?

It is recommended that the designated national regulatory authority provide target-oriented and continuous support for those educational institutions providing training programmes. Ways of drawing on the knowledge and expertise of regional, national or international medical–scientific organizations, as well as other stakeholders such as regulators from more advanced countries and consultants, should be considered, as this may offer an efficient route to building expertise.

Finally, it should be acknowledged that training and competence programmes are usually developed and implemented in a stepwise manner, starting with smaller pilot programmes of limited scope and working up – after periodic checks and evaluation – to more comprehensive training schedules covering a wider range of topics. However, there will always be a need for those delivering the training to have an in-depth knowledge of the regulatory environment. In this regard, and especially if trainers originate from another country, it is advisable to put in place a mechanism that facilitates direct dissemination and exchange of regulatory and laboratory expertise between the trainers and the trainees.

3.5 STEP 5
Implement and enforce regulations

The existence of a regulatory framework for biosafety and biosecurity by itself does not necessarily ensure a high degree of penetration and compliance with its statutory and non-statutory requirements. What is usually far more important is the manner in which its laws, regulations and guidelines are implemented and enforced.

3.5.1 Challenges in implementing the NBBF

The implementation of new or revised laws and regulations often proceeds differently from expected; it is highly likely that there will be barriers and challenges to implementation that will need to be overcome. However, anticipation and forward planning can help to avoid at least some roadblocks before they become major issues and hinder the implementation of the NBBF as planned.

Preparatory work conducted by the authors of this guidance, which included a review of recent literature and current practice, identified a number of common challenges faced by countries working to establish a more effective regulatory system for biosafety and biosecurity. For convenience, these challenges have been grouped into 10 broad categories, as detailed in Table 3.6. Countries are encouraged to bear this list in mind when planning the implementation of their regulatory framework.

Table 3.6 Implementing laboratory biosafety and biosecurity regulations and requirements: commonly encountered challenges

Country- or region-specific regulations, standards and guidelines
Limited access to biosafety and/or biosecurity regulatory framework
Adopting regulations from the other countries with little or no modifications
Absence or lack of translated biosafety and biosecurity resource materials and guidelines into local languages
Insufficient or inadequate technical support for developing and drafting policies, standards and guidance documents
Regulations/laws drafted without sufficient regard to evidence regarding the effectiveness of safety and security measures
No provision or mechanisms for "future-proofing" regulations and guidelines so that they keep pace with changes in technology
Limited dissemination of information about the new or revised regulations, standards and guidelines to all involved sectors and regions, in particular, those sectors and institutions whose operations and work practices will be affected
Biosafety and biosecurity awareness
Decision-makers and resulting policies demonstrate inadequate awareness about the international arrangements (e.g. Biological Weapons Convention), resolutions and protocols pertaining biosafety and biosecurity
Laboratory personnel lack the awareness about the existing policies/laws in their country
Inadequate understanding of the issue, and insufficient commitment and coordination from government
Lack of internal communication on biosafety and biosecurity (measures, initiatives, events) between relevant national stakeholders
Infrastructure
Deficiencies in the national infrastructure (e.g. power supply, roads and other transportation networks)
Over- designing and -engineering of biomedical laboratories **Note:** The existence of facilities which are over-specified relative to actual need risks placing undue financial pressures on the overall infrastructure budget
Difficulties in building and maintaining laboratories due to lack of financial resources

Table 3.6 Implementing laboratory biosafety and biosecurity regulations and requirements: commonly encountered challenges (continued)

Transport/import/export regulations
Absence or lack of approved carriers for external and internal transfer of specimens
Overly restrictive import/export and transport regulations involving multiple levels of bureaucracy which result in delays and burdensome paperwork
Excessive carrier and transportation costs
Training and skilled personnel
Inadequate numbers of trained and skilled personnel
Dearth of appropriate training resources or translated documents
Insufficient or absence of regular retraining programmes (refresher courses)
Biosafety and biosecurity data
Insufficient or lack of applied biosafety data (i.e. data on the effectiveness of the safety measures)
Inadequate reporting of incidents/accidents
Deficient disease monitoring systems
Equipment, reagents and services
Financial and technical constraints for maintaining equipment
Incorrect or inefficient use of the equipment
Nonadherence to good microbiological practice and procedures
Biological safety cabinets not certified periodically or not maintained properly
Insufficient availability of equipment, reagents and transportation in less accessible areas (i.e. outside major cities and towns)

Table 3.6 Implementing laboratory biosafety and biosecurity regulations and requirements: commonly encountered challenges (continued)

Risk assessment
"Novel" pathogens are initially classified and assumed to be high risk as a precautionary measure. This initial classification is rarely revisited which, unless the biological agent causes an outbreak overwhelming the public health system, could potentially lead to "over-management" of some biological agents and inefficient use or available resources.
Constraints on the capacity of laboratories to specify an acceptable level of risk, i.e. one that achieves an acceptable compromise in terms of protection of individual and public health on the one hand and the operational burden on the other.
Certification/accreditation
A dearth of qualified certifiers (independent of those who built the laboratory initially and those who are responsible for its ongoing maintenance
Confusion as to which standards should be used for certification
Use of often time-consuming accreditation schemes when other forms of external monitoring/surveillance control might be more appropriate in a given setting/ laboratory facility
Management processes, administrative controls and leadership
Absence or lack of culture of safety and responsibility in the facility
Shortage of safety officers, lack of safety guidelines and standard operating procedures (SOPs)
Managerial and administrative process required to implement biosafety and biosecurity practices not given sufficient priority
Lack of, or weak, leadership
Limited adoption of biosafety and biosecurity standards and guidelines by the laboratory
Absence or lack of waste management system and immunization programme for the laboratory personnel
Inadequate documentation and record-keeping systems in the laboratory
No electronic inventory or tracking system for biological specimens/samples
Insufficient preparedness for incidents (e.g. spills of infectious material, equipment failure, injuries)

3.5.2 Implementing the NBBF

The successful implementation of new or revised regulatory requirements as intended largely depends on how they are interpreted by the addressees.[3] Thus, in order to promote a common understanding and a harmonized approach to implementation, interpretative and supporting guidance should be provided as part of the NBBF. In providing detailed implementation information and guidance, particular attention should be given to the need for clear communication of the principles and practices of risk assessment, risk control and risk communication for biological agents.

It will also be necessary to mobilize and manage the necessary resources – financial, technical and human – that will be needed to ensure that the new regulations are implemented in a managed fashion. To a certain extent, the issue of the necessary resources will have been addressed and clarified as part of STEP 3. The pilot programme (see Section 3.3.3: Stakeholder involvement), in particular, should have identified what additional infrastructure and resources will be needed to be put in place ensure a smooth national roll out of the NBBF requirements.

Table 3.7 lists some key areas of implementation policy that need to be considered as part of STEP 5. These decision points are supplemented, where appropriate, with suggested policy options (based on country experience and current practice). Some additional issues that may need to be considered are also mentioned.

Table 3.7 Selected STEP 5 decision points and policy options, where appropriate

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Implementation	
Approach to harmonization	**Risk assessment functions** Depending on country circumstances, it may be preferable to establish agreement, either at the national, regional or subregional level, on the general principles of how to approach the evaluation of risk assessments rather than to adopt a more prescriptive approach that involves agreeing specific methodologies and information requirements for risk assessment and analysis (e.g. setting criteria for defining unacceptable risks). **Administrative and reporting functions** Administrative functions, which typically include documentation, information sharing, and reporting/ notification systems, again may be harmonized at either the national, regional or subregional (i.e. provincial) level, depending on country circumstances and preferences.

[3] In the context of STEP 5, the implementation step, "addressees" refers to the managers and staff of the biomedical laboratories who will be largely responsible for implementing the new or revised biosafety and biosecurity regulations at the local (i.e. facility) level.

Table 3.7 Selected STEP 5 decision points and policy options, where appropriate (continued)

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Requirements governing applications for approval (e.g. laboratory registration, handling of biological agents)	Specific parameters to consider may include: • time frame • documents and certifications needed (e.g. a quality management system or QMS) • procedures for delivering decisions • appeals process • fees (if any) • duration for approvals (i.e. these may be either time-limited or open-ended
Surveillance and monitoring	In terms of monitoring and surveillance functions (e.g. biological agent risk estimation, approval procedures, handling requirements), countries may choose to have: • no follow up for all microorganisms (least desirable) • minimum follow up for non-critical microorganisms • strong follow up for critical microorganisms A follow-up time period may be specified; follow up of < 5 years might be described as short term whereas periods > 5 years as long term.
Enforcement	
Enforcement and compliance	In terms of enforcement, consideration may be given stipulating: • levels of inspection and audit • fines and penalties for non-compliance

Good leadership is of pivotal importance to the successful and timely implementation of the biosafety and biosecurity regulatory framework. Implementers are thus strongly urged to invoke the "leadership principle": this requires leaders at all levels to establish a unity of purpose and direction and to create conditions in which staff are committed to achieving their organization's objectives. Although especially relevant to staff of biomedical laboratories – as major addressees of the NBBF – the leadership principle is also relevant to regulators and other stakeholder bodies such as the NBBC.

In keeping with the tenets of the leadership principle, heads of biomedical medical laboratories should be possessed of the necessary management skills and leadership qualities which will enable them to successfully establish a culture of trust and integrity,

encourage organization-wide commitment, and mobilize and match resources to specific tasks and activities. This will in turn strengthen the likelihood of an organization aligning its policies, processes and resources towards the achievement of its objectives, which in this context are the adoption of processes and procedures that conform to new or revised biosafety and biosecurity regulations. Strong and engaged leadership will also lead to an overall higher efficacy and efficiency in meeting regulatory compliance.

3.5.3 Implement stakeholder engagement and public awareness programmes

In the interests of ensuring transparency and acceptability, stakeholder participation and public engagement should be encouraged throughout the entire process of developing and implementing a NBBF, from the first through to the very last step (see also Section 3.3.3: Stakeholder involvement).

Within the context of this implementation step, opportunities for stakeholder participation and engagement may be engineered through formal requests for input and feedback on the proposed regulations and the implementation process. While the implementation phase represents a key opportunity for stakeholder consultation, the benefits of undertaking engagement activities earlier in the stepwise process, for example during policy development and constitution of advisory committees (such as the NBBC) (see STEP 1) and the regulatory framework design phase (see STEP 3), cannot be overstated. In this context, it may be noted that national and international standardization bodies provide helpful examples of good communication practice, as evidenced by the development of their (mostly voluntary) standards through a process of consensus.

3.5.4 Enforcement activities

In order to improve biosafety and biosecurity at the national level it will be necessary to have in place an effective programme – at least initially – for monitoring the implementation process, and then for the surveillance of compliance with the regulatory requirements. Both these regulatory activities should be included as integral parts of any regulatory framework for biosafety and biosecurity (see Table 3.7).

Ideally, the NBBC and the national regulatory authority (NRA) should take the lead in designing and developing an inspection system that, when systematically executed, will contribute much to confidence and acceptance of the new regulatory framework. Moreover, assuming sufficient resources have been devoted to STEP 4 (Strengthening regulatory expertise), the regulatory authorities responsible for the inspection and monitoring activities should have adequately qualified and trained staff available to perform these important functions.

In some countries, inspection and monitoring functions are performed exclusively by governmental authorities. Elsewhere, alternative approaches based on peer

evaluation systems (which employ suitably qualified assessors from, for example, either a third party or the nongovernmental sector) may be more appropriate and equally acceptable.

To facilitate the progressive adoption and implementation of new or revised regulations governing laboratory biosafety and biosecurity, it is recommended that facilities be allowed a period of transition, or a "grace" period, during which necessary changes to laboratory working practices can be incrementally introduced. Based on the experience of several countries, a reasonable transition period for biosafety and biosecurity legislation is three to five years: this however assumes that many of the necessary prerequisites are already in place.

Within this transition phase, biomedical laboratories could be permitted the option of applying future regulatory requirements on a voluntary basis for a specified period before mandatory actions are required. This too may be organized in a stepwise fashion, such that an initial voluntary reporting phase precedes a period during which reporting is mandatory before the final phase comes into force – the delivery of sanctions for non-compliance. Evaluation of the performance of the pilot implementation phase (see Section 3.3.3) conducted as part of STEP 3 will help to establish meaningful transition times and options combined with requirements that can be realistically fulfilled.

3.6 STEP 6
Establish national information exchange networks and international partnerships

The presence of efficient mechanisms of communication and information exchange between stakeholders will greatly enhance both implementation and continuous strengthening of the regulatory system for laboratory biosafety and biosecurity. It is therefore recommended that responsibility for establishing and maintaining communication networks be assigned to an appropriate body and that adequate resources be allocated to this function.

While it may be preferable to assign responsibility for information exchange to a single entity – for instance, the NBBC – that may not always be possible, especially if regulatory responsibility for biosafety and biosecurity is distributed among several agencies operating in different sectors (see Table 3.8). Under these circumstances, it is even more important for countries to develop the necessary administrative infrastructure to facilitate information exchange between the various regulatory agencies in different sectors. Key sectors to engage in information exchange networks might include the chemical or nuclear industry sector, especially in regard to biosecurity, and also the biomedical research sector. Indeed, in the longer term, intersectoral information exchange may well lead to wider collaboration and opportunities to integrate the regulation of activities involving biological agents across the human health, animal health and the security sectors, as well as foster good safety and security practices in the handling of all potentially hazardous substances.

The benefits of strong international relationships have been already been mentioned in the context of conducting a national evaluation of existing regulatory environment (see STEP 2). International collaboration will also support appropriate national action with regard to the provision of comprehensive training programmes and the development of surveillance concepts and diagnostic services for identifying new and emerging pathogens. In addition, international networking will promote an evidence-based approach for the identification of relevant risk pathways and will contribute to continuous harmonization of regulatory frameworks for laboratory biosafety and biosecurity.

To assist users to complete this penultimate step, Table 3.8 highlights some of the most pertinent decision points; various policy options are also suggested.

Table 3.8 Selected STEP 6 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Responsibility for establishing and maintaining national information exchange networks	Options include: • solely with the national biosafety and biosecurity committee (NBBC) • solely with the national regulatory authority (NRA) • shared between the NBBC and the NRA • distributed among other stakeholders medical-scientific organizations
Sectors and organizations to involve in information exchange (at the national and international level)	At the national level, information exchange participant might include: • regulatory authorities (in human health, animal health, environmental protection, food safety, defence) • scientific organizations • research organizations • industry At the international level, information exchange participants might include: • other WHO Member States • WHO and other United Nations agencies (e.g. Food and Agriculture Organization (FAO), World Organization for Animal Health (OIE) • partners of international programmes and initiatives such as Global Health Security Agenda (GHSA) and the Joint External Evaluation (JEE)

3.7 STEP 7
Review performance and adaptability to the national context and evolving risks

As per the principle of continual improvement, it is essential to evaluate the NBBF periodically to assess its performance and verify that it has achieved its intended impact. At the very least, any performance evaluation exercise should establish whether or not there has been an improvement in biosafety and biosecurity nationally. It should also assess the progress towards pre-specified goals and objectives achieved by the principal stakeholders (i.e. regulators and biomedical laboratories), and whether they were able to meet the new regulatory requirements in a reasonably feasible and sustainable manner.

Ideally, the NBBC should suggest a timeframe and methodology for conducting a formal review of the entire NBBF (see Table 3.9). It is also advisable to agree a set of criteria against which performance of the NBBF might be measured. Areas which should be covered by a performance review include the following:

- completeness and transparency of the regulatory framework
- responsiveness of the regulatory framework with regard to new research findings and newly-emerging risks
- competence of regulatory staff (this may be demonstrated, for example, by qualitative and quantitative data on training)
- effectiveness of monitoring and surveillance activities
- consistency and overall quality improvement of laboratory activities with regard to biosafety/biosecurity (this may be assessed, for instance, by reporting on the presence and availability of state-of-the-art laboratory instructions for purchasing, storage, handling, transport and disposal of biological agents)
- improvements in the safety of laboratory staff

In addition to routine performance reviews, circumstances may arise which necessitate an unscheduled evaluation of the NBBF, either in its in entirety or in part. In the field of biosafety and biosecurity, changes in the national scientific, economic, political and regulatory landscape which impact on the scope of regulatory control and thus precipitate a more urgent review of the regulatory system are not uncommon. Examples of such "regulatory triggers" include innovations in modern technology, newly-developing or emerging biological agents and their derivatives and – especially with regard to biosecurity – the development of technical capacities that have the potential to be misused and therefore constitute serious risks for public and individual health. Regulatory triggers might also stem from regional or international conventions and agreements justifying the need for a specific review and subsequent amendment of the national regulatory framework.

Table 3.9 provides an overview of the some of the decision points that typically need to be addressed as part of this final step of the stepwise approach to implementing a NBBF.

Table 3.9 Selected STEP 7 decision points and policy options

DECISION POINT(S)	POLICY OPTIONS/ADDITIONAL ISSUES TO CONSIDER
Timing of review/ evaluation of the NBBF for the purpose of verification of effectiveness and continual improvement	Options include: • performed during the transition period • performed once after initial implementation • performed periodically according to a pre-specified systematic procedure/method • performed as and when triggered by certain events relevant for biosafety/biosecurity issues • performed both periodically and as and when triggered by external circumstances
Responsibility for initiating and setting the criteria for the periodic review of the NBBF	Options include: • national biosafety and security committee • national regulatory authority or authorities according to a commonly agreed approach • nongovernmental organizations, such as laboratory professional organizations or medical–scientific organizations

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ANNEX I

Glossary of terms

For the purposes of this document, the following definitions and descriptions apply. These terms may have different meanings in other contexts.

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

Biomedical laboratories: Healthcare, clinical, diagnostic or medical laboratories, public health laboratories, veterinary laboratories, research centres, biobanks, pharmaceutical and all other types of facilities that handle and/or store hazardous biological agents.

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

Hierarchy of legislation: means the ranking of the legal instruments as prescribed under the fundamental law (e.g. the constitution) of a country.

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

Laboratory biosafety: The containment principles, technologies and practices that are implemented to prevent the unintentional exposure to biological agents or their accidental release in biomedical laboratories.

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

Microorganism: Microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material.

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

Primary legislation: The legal instruments issued by the legislative body of a country (i.e. laws/acts).

Regulatory framework: The system of internationally and nationally binding legislation such as laws and regulations amended and specified by voluntary, best-practice standards, guidelines and/or recommendations.

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

Risk assessment: A systematic process of gathering and evaluating information to support a risk-management process.

Secondary legislation: means the legal instruments, i. e. regulations, issued by the executive body of a country under the authority of primary legislation.

Soft law: instruments containing influential provisions, which are not legally binding, e.g. national or international standards, guidelines and recommendations.

Stakeholder: means a person, group, or organization that can affect or be affected by the impacts of the regulatory framework.

ANNEX II

Examples of biosafety and biosecurity legislation and soft law in selected WHO Member States

Introduction

The following country tables list the legislation and soft law (including standards) adopted by selected WHO Member States for regulating laboratory biosafety and biosecurity. References to the national instruments in this document do not imply approval or endorsement by WHO, but give an overview of the regulatory frameworks adopted by the Member States and provide information only to State Party officials when developing or revising regulations in their national contexts. It should be noted that this list is non-exhaustive list. Links to the respective legal instruments are provided to aid further reading and exploration. Web links were valid as of 23rd March 2020.

General note: In most countries, standards are not considered legally binding. However, they reflect the current state-of-the-art with regard to the topic addressed through the standard. Sometimes, regulators might tie the use of a standard to legislation to make the application of a standard mandatory. This list does not inform about the liability of standards within a Member States' regulatory framework.

AUSTRALIA	
Act(s)	
• **The Gene Technology Act (2000)**	Available in English at: https://www.legislation.gov.au/Details/C2016C00792
• **National Health Security Act (2007)**	Available in English at: https://www.legislation.gov.au/Details/C2016C00847
• **Biosecurity Act (2015)**	Available in English at: https://www.legislation.gov.au/Details/C2017C00303
Regulations	
• **The Gene Technology Regulation (2001)**	Available in English at: https://www.legislation.gov.au/Details/F2016C00615
• **National Health Security Regulations (2008)**	Available in English at: https://www.legislation.gov.au/Details/F2010C00436
• **Biosecurity Regulation (2016)**	Available in English at: https://www.legislation.gov.au/Details/F2016L00756
Standards	
• **AS/NS 2243.3:2010 Safety in laboratories: Microbiological safety and containment Security Sensitive Biological Agents Standards**	Available in English at: http://www.health.gov.au/ssba#standards

Guidelines, recommendations and other soft law	
• **Guidelines in relation to genetically modified organisms**	Available in English at: http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/content/guidelines-1
• **Security Sensitive Biological Agents standards & guidelines**	Available in English at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ssba-guidelines.htm
• **Security Sensitive Biological Agents Standards Fact Sheets**	Available in English at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ssba-factsheets.htm
Other relevant legislation	
• **Australian Code for the Transport of Dangerous Goods by Road and Rail, Civil Aviation Safety Regulations, Agricultural and Veterinary Chemicals (Administration) Act (1992)** • **Agricultural and Veterinary Chemicals Code Act (1994)** • **Therapeutic Goods Act (1989) and the Therapeutic Goods Regulations (1990)**	

CANADA	
Act(s)	
• **Human Pathogens and Toxins Act (S.C. 2009, c. 24)**	Available in English at: http://lois-laws.justice.gc.ca/eng/acts/H-5.67/index.html/
• **Health of Animals Act (S.C. 1990, c.21)**	Available in English at: http://lois-laws.justice.gc.ca/eng/acts/H-3.3/
Regulations	
• **Human Pathogens and Toxins Regulations (SOR/2015-44)**	Available in English at http://lois-laws.justice.gc.ca/eng/regulations/SOR-2015-44/index.html
• **Health of Animals Regulations (C.R.C., c. 296)**	Available in English at: http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._296/
Standards	
• **Canadian Biosafety Standard**	Available in English at: https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/second-edition.html

Guidelines, recommendations and other soft law	
• **Canadian Biosafety Handbook**	Available in English at: https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/handbook-second-edition.html
• **Canadian Biosafety Guidelines**	Available in English at: https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/guidance.html
• **Directives, Advisories and notifications**	Available in English at: https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/biosafety-directives-advisories-notifications.html
• **An Analytical Approach: biosafety and biosecurity oversight framework**	Available in English at: https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/analytical-approach.html
Other relevant legislation	
• **Export and Import Permits Act** • **Quarantine Act** • **Transportation of Dangerous Goods Act** • **Chemical Weapons Convention Implementation Act** • **Customs Act/Canada Border Services Agency Act** • **Criminal Code of Canada** • **Hazardous Products Act** • **Department of Public Safety and Emergency Preparedness Act/Emergency Management Act**	

EUROPEAN UNION	
Directives	
• **Directive 2000/54/EC: Protection of workers from risks related to exposure of biological agents at work**	Available in English at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32000L0054
• **Directive 2009/41/EC: Contained use of Genetically modified microorganisms regulation (EC) No 1946/2003: Transboundary movements of Genetically modified micro-organisms**	Available in English at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32009L0041
• **Directive Council Directive 94/55/EC: On the approximation of the laws of the Member States with regard to the transport of dangerous goods by road**	Available in English at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32006L0089
• **Council Directive 96/49/EC: On the approximation of the laws of the Member States with regard to the transport of dangerous goods by rail**	Available in English at: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32006L0090

GERMANY	
Rules	
• **Technical Rules for Biological Agents TRBA**	Available in English at: https://www.baua.de/EN/Service/Legislative-texts-and-technical-rules/Rules/TRBA/TRBA.html

KENYA	
Act(s)	
• **National Biosafety Act, 2009**	Available in English at: http://www.biosafetykenya.go.ke/index.php?option=com_content&view=article&id=16&Itemid=121
• **The Science and Technology Act–Chapter 250 (1980, revised 2009)**	Available in English at: http://www.kenyalaw.org/kl/fileadmin/pdfdownloads/Acts/ScienceandTechnologyAct_Cap250.pdf
• **Occupational Safety and Health Act, 2007**	Unofficial version available in English at https://www.ilo.org/dyn/natlex/docs/SERIAL/78264/83534/F789589155/KEN78264.pdf
Regulations	
• **Contained Use Regulations**	Available in English at: http://www.biosafetykenya.go.ke/index.php?option=com_content&view=article&id=17&Itemid=122
• **Environmental Release Regulations**	Available in English at: http://www.biosafetykenya.go.ke/Docs/The%20Biosafety%20(Environmental%20Release)%20Regulations,%202011(2).pdf
• **Export, Import and Transit Regulations**	Available in English at: http://www.biosafetykenya.go.ke/index.php?option=com_content&view=article&id=17&Itemid=122
Policies	
• **National Biotechnology Development Policy, 2006**	Unofficial version available in English at: bch.cbd.int/database/attachment/?id=18881

Guidelines, recommendations and other soft law	
• **Laboratory Biosafety and Biosecurity Policy Guidelines**	Unofficial version available in English at: https://internationalbiosafety.org/wp-content/uploads/2019/08/Kenya-Biosafety-Guidelines.pdf
• **Guidelines and checklists for the risk assessment and certification of facilities dealing with genetically-modified organisms**	Available in English at: http://www.biosafetykenya.go.ke/index.php?option=com_content&view=article&id=18&Itemid=123
• **Guidelines for testing of genetically modified organisms in certified laboratories**	Available in English at http://www.biosafetykenya.go.ke/index.php?option=com_content&view=article&id=18&Itemid=123

RUSSIA	
Regulations	
• **Regulations on Handling Microorganisms in Pathogenicity Groups 3, 4**	Unofficial version available in English at: http://www.vertic.org/media/National%20Legislation/Russian_Federation/RU_Regulations_Handling_Microorganisms.pdf

SOUTH AFRICA	
Act(s)	
• **National Health Act (Act 61 of 2003)**	Available in English at: https://www.gov.za/documents/national-health-act
• **National Health Amendment Act (2013)**	Available in English at: https://www.gov.za/documents/national-health-amendment-act
• **Occupational Health and Safety Act (Act 85 of 1993)**	Available in English at: https://www.gov.za/documents/occupational-health-and-safety-act
• **Non-Proliferation of Weapons of Mass Destruction Act (Act 87of 1993)**	Available in English at: https://www.ctbto.org/fileadmin/user_upload/pdf/Legal_documents/national_provisions/SouthAfrica_NonProliferationofWeaponsofMassDestruction_020793.pdf
• **Hazardous Substances Act (Act 15 of 1973)**	Available in English at: https://www.gov.za/documents/hazardous-substances-act-16-apr-2015-1120
• **Genetically Modified Organisms Act [No. 15 of 1997)**	Available in English at: https://cer.org.za/virtual-library/legislation/national/biodiversity-and-conservation/genetically-modified-organisms-act-15-of-1997
• **Animal Health Act (Act 7 of 2002)**	Available in English at: https://www.gov.za/documents/animal-health-act

Regulations	
• **National Health Act (Act 61 of 2003) Regulations relating to the registration of microbiological laboratories and the acquisition, importation, handling, maintenance and supply of human pathogens**	Available in English at: https://www.gov.za/sites/default/files/gcis_document/201409/35099rg9699gon178.pdf
• **Occupational Health and Safety Act (Act 85 of 1993) Regulations for Hazardous Biological Agents (R1390) (2001).**	Available in English at: http://www.labour.gov.za/DocumentCenter/Regulations%20and%20Notices/Regulations/Occupational%20Health%20and%20Safety/Regulation%20-%201390%20-%20OHS%20-%20Hazardous%20Biological%20agents.pdf
• **National Health Act (Act 61 of 2003). Regulations relating to the use of Human Biological Material (R177) (March 2012)**	Available in English at: https://www.gov.za/documents/national-health-act-regulations-use-human-biological-material
Policies	
• **The National Infection Prevention and Control (2007)**	Available in English at: http://policyresearch.limpopo.gov.za/handle/123456789/888

THAILAND	
Act(s)	
• **Pathogens and Animal Toxins Act, B.E. 2558 (2015)**	Unofficial English translation available at: http://www.vertic.org/media/National%20Legislation/Thailand/TH_Hazardous_Substance_Act.pdf
• **Hazardous Substance Act, B.E. 2535. Animal Epidemics Act, B.E.2499 (1956)**	Unofficial English translation available at: http://www.vertic.org/media/National%20Legislation/Thailand/TH_Animal_Epidemics_Act.pdf
• **The Communicable Disease Act, B.E. 2523**	Unofficial English translation available at: http://www.vertic.org/media/National%20Legislation/Thailand/TH_Disease_Act.pdf
Guidelines, recommendations, and other soft law	
• **Biosafety Guidelines for Contained Use of Genetically Modified Microorganisms at Pilot and Industrial Scales**	Available in English at: http://www.biotec.or.th/en/index.php/info-center/publications/1149-biosafety-guidelines-for-contained-use-of-genetically-modified-microorganisms-at-pilot-and-industrial-scales
Other relevant legislation	
Arms Control Act, B.E. 2530 (1987)	

UNITED STATES OF AMERICA	
Act(s)	
• **Public Health Security and Bioterrorism Preparedness and Response Act of 2002**	Available in English at: https://www.congress.gov/bill/107th-congress/house-bill/3448/text
• **Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA Patriot Act) Act of 2001**	Available in English at: https://grants.nih.gov/grants/policy/select_agent/Patriot_Act_2001.pdf
• **Occupational Safety and Health Act of 1970**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=OSHACT&p_id=2743
Regulations	
• **Select Agent Regulations**	Available in English at: https://www.selectagents.gov/regulations.html
• **Animal and Animal Product Import and Export regulations and guidelines**	
• **Import Regulations for Infectious Biological Agents, Infectious Substances, and Vectors**	Available in English at: https://www.govinfo.gov/content/pkg/CFR-2014-title42-vol1/pdf/CFR-2014-title42-vol1-sec71-54.pdf
• **Department of Transport regulations (49 CFR 171 - 178)- Hazardous Materials Regulations**	Available in English at: https://www.gpo.gov/fdsys/pkg/CFR-2011-title49-vol2/pdf/CFR-2011-title49-vol2.pdf

Standards	
• **42 USC 262-Licensing of biological products and clinical laboratories. Subpart 1--Biological Products**	Available in English at: https://www.selectagents.gov/resources/42USC262.pdf
• **29 CFR 1910.1200-Hazard Communication**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=10099
• **29 CFR 1910.1450-Occupational Exposure to Hazardous Chemicals in the Laboratory**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=10106&p_table=STANDARDS
• **The Personal Protective Equipment (PPE) standard 29 CFR 1910.132)**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=9777&p_table=STANDARDS
• **The Blood borne Pathogens standard (29 CFR 1910.1030)**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=10051&p_table=STANDARDS
• **The Eye and Face Protection standard (29 CFR 1910.133)**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9778
• **The Respiratory Protection standard (29 CFR 1910.134)**	Available in English at: https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=12716
Policies	
• **DURC Policy (DURC;Dual Use Research of Concern)**	Available in English at: http://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf
• **Policy for Institutional Oversight of Life Sciences DURC**	Available in English at: http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf
• **Policies on Biosafety, Biosecurity, and Emerging Biotechnology**	Available in English at: https://osp.od.nih.gov/biosafety-biosecurity-and-emerging-biotechnology/

Guidelines, recommendations, and other soft law	
• **Biosafety in Microbiological and Biomedical Laboratories (BMBL)**	Available in English at: https://www.cdc.gov/labs/BMBL.html
• **NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)**	Available in English at: https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf
• **Standard Operating Procedure for OPP Microbiology Laboratory Personnel Training**	Available in English at https://www.epa.gov/sites/production/files/2015-02/documents/adm-04-04.pdf
• **Standard Operating Procedure for Use and Maintenance of Biological Safety Cabinets**	Available in English at: https://www.epa.gov/sites/production/files/2014-12/documents/qc-06-05.pdf
• **Restricted Experiments Guidance**	Available in English at: https://www.selectagents.gov/resources/Restricted_Experiment_Guidance.pdf
• **Federal Select Agent Program: Plan and Personnel Guidance**	Available in English at: https://www.selectagents.gov/compliance.html
• **Guidelines for Biosafety Laboratory Competency (2011)**	Available in English at: https://www.cdc.gov/mmwr/preview/mmwrhtml/su6002a1.htm
• **Laboratory Safety Guidance**	Available in English at: https://www.osha.gov/Publications/laboratory/OSHA3404laboratory-safety-guidance.pdf

ANNEX III

WHO assessment tool

Supports WHO's recommended stepwise approach to implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories

Introduction

Purpose of the WHO assessment tool

The purpose of this tool, which takes the form of a structured checklist, is to facilitate the assessment of national regulatory capacity in the field of biosafety and biosecurity. In addition to providing a basis for a detailed and an impartial evaluation of existing regulatory strategies, structures and available resources, this tool is also designed to support regulators and policy-makers in developing and implementing a comprehensive regulatory framework for managing the activities of biomedical laboratories from the point of view of ensuring national biosafety and biosecurity. For this reason, the main part of the assessment tool is intentionally aligned to the recommended stepwise approach to implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories, as outlined in the main part of the guidance document to which this tool is annexed.

As this assessment tool is intended to be used in conjunction with the WHO recommended stepwise approach to implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories, it is targeted at policy-makers and national regulators. As the intended primary users, national regulators and staff of relevant agencies and institutions tasked with developing biosafety and biosecurity regulatory requirements are thus directed to the columns labelled "Self-assessment". However, the tool may also be used by external consultants and assessors for review and consultancy purposes, for whom the last column (headed "Eternal review") may be more appropriate.

Users of this tool may find it helpful to consult other related WHO guidance documents and tools, for example the WHO Laboratory Assessment Tool (LAT)*(1)* or the Joint External Evaluation (JEE) tool *(2)*. The former, published in 2012, describes a general process for conducting an assessment of the functionality of the national health laboratory system and provides a set of downloadable questionnaires to help facilitate this task, both at the national system level (LAT: Annex 1) and at the level of individual laboratories (LAT: Annex 2). In the context of this guidance document, special attention might be drawn to Chapter 8 (on biological risk management) of Annex 1 (the system questionnaire). Within the JEE tool, which is used to assess the capacity of WHO Member States to prevent, detect and rapidly respond to public health threats in accordance with the International Health Regulations (IHR), indicators 6.1 and 6.2 (which relate to national biosafety and biosecurity systems) are likely to be of particular interest to users of this guidance .

Notes for users

This assessment tool is composed of different parts: Section A, titled "General information", precedes a set of structured questions designed to guide an initial situational analysis of the existing regulatory environment governing biosafety and biosecurity (Section B). Finally, Section C guides users through the recommended stepwise process for developing and implementing a regulatory framework for laboratory biosafety and biosecurity. To this end, the questions posed in Section C of the assessment tool are intended to reflect the range of policy options, opportunities and challenges that users are likely to encounter as they progress through each of the seven steps of the recommended approach to regulating laboratory biosafety and biosecurity.

In keeping with other WHO guidance documents that deal with biosafety and biosecurity *(1)*, possible answers to the questions posed in this assessment tool (unless otherwise advised) may be coded as follows:

1 = Yes,

2 = Partial,

3 = No, or

4 = Not applicable.

Open questions, to which necessary and additional information may be provided, are indicated in italics. Users of this tool are encouraged to provide as much explanatory information as possible as this will assist greatly in the task of gaining a comprehensive understanding of the regulatory framework, including all its interrelated elements.

References

1. WHO/GCR. Laboratory assessment tool. Geneva: World Health Organization, 2012 (WHO/HSE/GCR/LYO/2012.2) (https://www.who.int/ihr/publications/laboratory_tool/en/, accessed 7 January 2020).

2. Joint external evaluation tool: International Health Regulations (2005), second edition. Geneva: World Health Organization; 2018 (https://www.who.int/ihr/publications/WHO_HSE_GCR_2018_2/en/,accessed 7 January 2020).

SECTION A. General Information

Country assessed:	
Date(s) of the assessment (DD/MM/YYYY):	
Name and contact details of the person(s) responsible for conducting the assessment:	
Name, contact details and position/affiliation of the person(s) consulted during the course of the assessment, if applicable:	
Comments:	

SECTION B. Situational analysis

Notes to users

1. Possible responses (unless otherwise advised):

   1 = yes

   2 = partial

   3 = no

   4 = not applicable

2. For additional information and questions, users may like to also consult Annex 1 of the WHO Laboratory Assessment Tool (the system questionnaire), in particular Chapter 8, and/or the Joint External Evaluation tool, in particular indicators 6.1 and 6.2 of which relate to national biosafety and biosecurity systems.

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
Hierarchy and structure of the elements of the existing regulatory framework					
0.1	Are biomedical laboratories currently regulated in any way with regard to biosafety issues?				
0.2	Are biomedical laboratories currently regulated in any way with regard to biosecurity issues?				
0.3	Does the current framework refer to binding primary and/ or secondary legislation (i.e. statutory laws and regulations, respectively) or to "soft law" (e.g. guidelines, technical standards, recommendations)?				
Scope and focus of the existing regulatory framework					
0.4	In which legal context are biomedical laboratories currently regulated? For instance, do laws and regulations cover employee protection, misuse of biological agents, laboratory quality and/or other sectors such as agriculture and transport?				
0.5	If a regulatory framework for biosafety and biosecurity is in place, is there separate or common legislation for biosafety and biosecurity?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
0.6	If laws and/or regulations are currently in place, do these primarily cover naturally-occurring disease agents (e.g. Mycobacterium tuberculosis or Ebola virus) or do they also include genetically-modified organisms (GMOs)?				
Profiling of biological agents					
0.7	Is there any form of biosafety profiling or risk categorization system in use (e.g. a pathogen risk group classification)?				
0.8	If the answer to Q0.7 is yes, please specify the profiling/ categorization system currently in use for assigning biological agents to a biosafety level.				
0.9	If the answer to Q0.7 is yes, is the assignment of microbiological agents to a biosafety level based on a risk assessment process?				
0.10	If the answer to Q0.9 is yes, is the risk assessment performed at: • the national level? • the regional level? • the facility/laboratory level (i.e. taking into consideration the individual factors at the facility)?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
0.11	Is there a list of biological agents (pathogens) that are subject to regulation?				
0.12	If the answer to Q0.11 is yes, is this list periodically updated?				
Containment of biological agents					
0.13	Do existing laws and/or regulations make provision for the safe storage and containment of biological agents?				
0.14	If the answer to Q0.13 is yes and containment is currently the subject of regulation, does the level of containment reflect the risk group of the biological agent?				
Organization of regulatory oversight					
0.15	Is there a mechanism in place to ensure regulatory oversight of the criteria for biosafety to be fulfilled by biomedical laboratories? **Note:** responsibility for regulatory oversight may lie with a single body or with several bodies.				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
0.16	Is there a mechanism in place to ensure regulatory oversight of the criteria for biosecurity to be fulfilled by biomedical laboratories? **Note:** responsibility for regulatory oversight may lie with a single body or with several bodies.				
0.17	If the responsibilities for biosafety and biosecurity regulatory oversight lie with more than one regulatory body, are those responsibilities well defined and communicated/ transparent to all stakeholders?				
Licensing, registration and notification systems					
0.18	Is there a requirement for the licensing, registration and/ or inspection of biomedical laboratories?				
0.19	Is there an independent notification system in place which authorizes laboratories to work with specific biological agents?				
Accident and reporting systems					
0.20	Is there a reporting system for accidents and incidents?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
0.21	If the answer to Q0.21 is yes, are the accident/incident reporting procedures sufficiently well defined and transparent to all stakeholders?				
Risk management systems					
0.22	Are the rules/regulations or guidance governing the assessment and management of biological risks at biomedical laboratories adequate?				
"One health" approach					
0.23	Are regulatory requirements and/or structures shared (or at least overlapping) between the human and veterinary health sector?				
0.24	If the answer to Q0.23 is yes, which regulations and/ or guidance and regulatory institutions are part of these shared (or overlapping) structures?	X			
Implementation strategies					
0.25	If guidance for the implementation of regulatory requirements for biomedical laboratories is already in place, is it published, regularly reviewed and effectively communicated to all stakeholders?				

SECTION C. Stepwise approach to regulating laboratory biosafety and biosecurity

Notes to users

1. Possible responses (unless otherwise advised):

   1 = yes

   2 = partial

   3 = no

   4 = not applicable

STEP 1
Mobilize national commitment and resources for the development and implementation of a national biosafety and biosecurity policy

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
National commitment to biosafety and biosecurity					
1.1	Has the national government made any formal dedication or declaration of its intent with regard to biosafety, for example, in the form of a vision and/or mission statement?				
1.2	Has the national government made any formal dedication or declaration of its intent with regard to biosecurity, for example, in the form of a vision and/or mission statement?				
National policies governing biosafety and biosecurity					
1.3	Is biosafety and biosecurity at biomedical laboratories the subject of a national policy?				
1.4	If the answer to Q1.3 is yes, is this national policy currently:				
1.4.1	• under development?				
1.4.2	• in the implementation phase?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
1.4.3	• well established and communicated to all stakeholders?				
1.5	If the answer to Q1.3 is yes, please provide the name(s), terms of reference and contact details of the organization/unit and responsible person(s) that have developed, implemented and/or communicated the national policy for laboratory biosafety and biosecurity.				
1.6	If the answer to Q1.3 is yes, does it represent an unambiguous commitment to biosafety and biosecurity?				
1.7	If the answer to Q1.3 is yes, is it consistent with the national policy for laboratory quality (if such a policy exists)?				
1.8	If the answer to Q1.3 is yes, is the national policy for laboratory biosafety and biosecurity:				
1.8.1	• a standalone document?				
1.8.2	• integrated into the national laboratory quality policy,				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
1.8.3	• integrated into another policy/regulation governing areas such as food, agriculture, environment, and/or human/animal health?				
1.9	If there is an established national policy for biosafety and biosecurity, does it provide a set of principles to guide the subsequent development and implementation of the regulatory framework for biosafety and biosecurity?				
Resources for biosafety and biosecurity policy development					
1.10	If a national policy does NOT currently exist, which capacities of the country could support the design process of a national policy for laboratory biosafety and biosecurity with regard to:				
1.10.1	• the legal requirements?				
1.10.2	• the scientific requirements (e.g. academic organizations, medical-scientific societies, universities)?				
1.10.3	• the technical requirements (e.g. occupational unions, professional organizations for laboratory technicians)?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
Supporting institutional structures and capacities					
1.11	Is there a national biosafety and biosecurity committee (or equivalent organization) that deals with the question of the management of biosafety and biosecurity at biomedical laboratories?				
1.12	If the answer to Q1.11 is yes, is this committee (or equivalent organization) supported by a competent national authority (e.g. a national regulatory agency or authority)?				
1.13	If the answer to Q1.12 is yes, please indicate the name, location and main responsibilities of this supporting competent national authority.				
1.14	If the answer to Q1.11 is yes, does the membership of the national biosafety and biosecurity committee (or equivalent organization) currently include:				
1.14.1	• regulators?				
1.14.2	• laboratory scientists?				
1.14.3	• physicians?				
1.14.4	• national security representatives?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
1.14.5	• (occupational) health organizations				
1.14.6	• providers of national (health) databases?				
1.14.7	• parties reflecting the cooperation between the human and animal/ environmental health sectors?				
1.15	If the answer to Q1.11 is yes, has the national biosafety and biosecurity committee (or equivalent organization), been instrumental in:				
1.15.1	• carrying out a situational analysis?				
1.15.2	• capacity building and training activities?				
1.15.3	• the development, improvement and implementation of the regulatory framework with regard to laboratory biosafety and biosecurity?				

STEP 2
Conduct a national evaluation and surveys

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
2.1	Have any evaluations or surveys related to the question of laboratory biosafety and biosecurity been conducted during the last 3–5 years?				
2.2	If the answer to question Q2.1 is yes, were the evaluations or surveys coordinated by the national biosafety and biosecurity committee?				
2.3	If evaluations or surveys have been carried within the last 5 years out but did not involve the national biosafety and biosecurity committee (or at least not exclusively), which institution(s) or unit(s) were responsible for the organization and conduct of those evaluations or surveys?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
2.4	Have any national, subnational or regional reviews, evaluations or surveys of specific aspects of laboratory biosafety and biosecurity been conducted during the last 3–5 years? Please provide relevant information in the corresponding column for each of the following components of laboratory biosafety and biosecurity:				
2.4.1	• existing human and scientific infrastructure including training programmes (e.g. training programmes for safe use of microorganisms)				
2.4.2	• current status of biotechnology and biological agent handling (e.g. type and quantities of GMOs)				
2.4.3	• existing financial concepts (e.g. for the installation and monitoring of biosafety and biosecurity concepts)				
2.4.4	• existing reporting system databases				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
2.4.5	• existing regulatory structures and legislation				
2.4.6	• existing mechanisms for the development of legislation and "soft law", including administrative and enforcement capacities				
2.4.7	• current stakeholders (e.g. representatives of various types of biomedical laboratories, medical-scientific organizations, regulatory bodies)				
2.4.8	• public opinion regarding the use, transport and storage of biological agents				
2.4.9	• existing mechanisms for regional cooperation and regulatory harmonization (e.g. within economic or regulatory alliances)				
2.5	Would you consider that the existing reviews and evaluations provide an impartial and comprehensive characterization of the national situation with regard to laboratory biosafety and biosecurity?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
2.6	If the answer to question 2.5 is no, how could the comprehensiveness and impartiality of available data and information relating to laboratory biosafety and biosecurity in the country be improved? For example, is there a need for a new evaluation or surveys?				
2.7	If there is a perceived for a new evaluation or further surveys, who would be responsible for undertaking such a task or tasks?				

STEP 3
Establish national institutions and operational mechanisms and develop best-fitting regulations

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
National institutions and operational mechanisms					
3.1	Have all existing institutions with regulatory responsibilities in the field of biosafety and biosecurity been identified (see STEP 2)?				
3.2	For those institutions which have been identified as having regulatory responsibility for biosafety and security, have their legally-anchored functions and responsibilities been adequately characterized (see STEP 2)?				
3.3	If the answer to Q3.2 is yes, does this characterization include information about any gaps or overlap that might exist in the regulatory system?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
3.4	Do the existing institutions and their regulatory functions cover the following activities (with regard to biomedical laboratory biosafety and biosecurity):				
3.4.1	• Legislation?				
3.4.2	• Enforcement?				
3.4.3	• Surveillance, monitoring and reporting?				
3.4.4	• Inspection services?				
3.4.5	• Diagnostic services?				
3.4.6	• Emergency repsonse (for example to disease outbreaks and major spills)?				
3.4.7	• Scientific research and advice?				
3.5	If several institutions or agencies have regulatory responsibilities for biosafety and biosecurity, how is the coordination among these institutions promoted in order to eliminate gaps, overlaps and potential conflicts in the regulatory system?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
3.6	If existing legal and institutional frameworks are to be used for the development and/or improvement of the national biosafety and security framework (NBBF), will a national biosafety and biosecurity committee (or equivalent body) be established and/or empowered by law to exercise an oversight and coordinating role with respect to the functions of the existing institutions?				
3.7	If existing legal and institutional frameworks are NOT going to be used for the development and/or improvement of the national biosafety and security framework (NBBF), will a new regulatory body be established (at a supra-ministerial level)?				
3.8	If a new regulatory body is to be established what characteristics will this new body have? **Note:** The response to this open question should address some of the issues raised by preceding questions (in particular Q3.4 and Q3.5) and for instance describe how this new body would interact with existing regulatory bodies, and whether and how this body will be involved in legislation, registration and/or inspection activities.				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
The regulatory framework					
3.9	Will the proposed national framework be entirely newly-developed or will it replace an existing framework (i.e. will it be based on existing legal and institutional frameworks but with amendments to address any gaps or shortcomings in the system, as appropriate)?				
3.10	Will the proposed national framework require amendments to existing legislation?				
3.11	Will the proposed national regulatory framework require new primary and/ or secondary legislation (i.e. legally-binding laws and regulations)?				
3.12	Will the proposed national regulatory framework require new non-legally binding standards and guidelines?				
3.13	Have any elements of the proposed national regulatory framework, in particular new primary and/or secondary legislation, previously been covered by legally non-binding guidelines?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
3.14	If the answer to Q3.13 is yes, please specify those guideline(s).				
3.15	Is the proposed national regulatory framework based on an evidence- and risk-based approach to risk management?				
3.16	Does the proposed national regulatory framework incorporate the following elements and concepts:				
3.16.1	• Registration and licensing procedures?				
3.16.2	• Incident reporting?				
3.16.3	• Transportation of biological material and infectious substances?				
3.16.4	• Biosafety programme management?				
3.16.5	• Monitoring and surveillance?				
3.16.6	• Laboratory biosecurity?				
3.16.7	• Waste management?				
3.16.8	• Integration within the "One Health" concept?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
3.16.9	• Information exchange/ capacity building?				
3.16.10	• Flexibility of the regulatory framework in response to current state of the art technologies?				
3.17	Does the proposed national regulatory framework make adequate provision for appropriate transitional periods? **Note:** A transitional period is usually specified to allow laboratories time to adapt their existing working practices to meet the requirements of any newly-developed rules and regulations or guidelines.				
Stakeholder engagement and involvement					
3.18	Will the national biosafety and biosecurity committee (or equivalent organization) be involved in the development and/or review of the proposed national regulatory framework?				
3.19	If the answer to Q3.18 is yes, please specify how the national biosafety and biosecurity committee (or equivalent organization) will be involved in the development and/or review of the national regulatory framework.				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
3.20	Will the public be involved in development and/or review of the proposed national regulatory framework? **Note:** Opportunities for public engagement may be provided through formalized requests for public input, but also by other mechanisms such as representation on advisory committees and other bodies, public hearings and individual involvement in the development of regulations and guidelines.				
3.21	If the answer to Q3.20 is yes, please specify how the public will be involved in the development and/or review of the national regulatory framework.				

STEP 4
Strengthen expertise to support implementation of a suitable regulatory system

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
4.1	Having training programmes delivered sufficient knowledge and expertise within the agencies and institutions with regulatory responsibilities in order to:				
4.1.1	• Analyse the findings of reviews and surveys of existing in-country regulatory expertise (see STEP 2)?				
4.1.2	• Identify and evaluate gaps and needs in in-country regulatory expertise?				
4.1.3	• Decide on the priorities and key components of the NBBF?				
4.2	Are education and training activities aimed at staff of competent authorities periodically scheduled and combined or linked with the national approach to regulating laboratory biosafety and biosecurity?				

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
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4.3	Are education and training activities aimed at staff of competent authorities periodically assessed and adjusted to meet the specific needs of the regulatory framework for biosafety and biosecurity?				
4.4	Does the national regulatory authority provide target-oriented and continuous support to those institutions that are responsible for organizing the training programmes?				
4.5	Are available informational resources and learnings from regional, national and international medical–scientific organizations and other stakeholders (e.g. regulators, consultants) integrated into the national and regional training programmes aimed at the relevant affected parties?				
4.6	Do planned training programmes consider the continuous need for trained individuals?				

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4.7	Do planned training programmes address the following key elements:				
4.7.1	• Coordination of risk assessment activities at the national, regional and subregional level?				
4.7.2	• Recruitment methods for national and international experts for training activities?				
4.7.3	• Best practice in the management of core competencies in risk assessment?				
4.7.4	• Scientific and technological advances and developments (e.g. in terms of GMO detection and monitoring) and their incorporation into the evidence-based risk assessment mechanism?				
4.7.5	• Training and qualification of government department and agency staff in risk assessment activities and programmes?				

STEP 5
Implement and enforce regulations

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
Implementation programme					
5.1	Does the NBBF provide detailed interpretative guidance and information regarding the regulatory requirements?				
5.2	If the answer to Q5.1 is yes, does the interpretative guidance promote a common understanding and a harmonized approach to implementation among all affected parties?				
5.3	If the answer to Q5.1 is yes, does the interpretative guidance pay sufficient attention to the explanation and communication of the principles and practices of risk assessment, risk control and risk communication for biological agents?				
5.4	Does the implementation programme adequately consider the existing financial, technical, and human resource challenges in the country?				

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5.5	Does the implementation programme include a consultative period (i.e. a period during which the implementation of new (or amended) regulations and guidelines is piloted in selected settings prior to national roll out)?				
5.6	Does the implementation programme provide suitable tools for the assessment of the introduction of new (or amended) regulations and guidelines in selected settings during the consultative period?				
5.7	Does the implementation programme make adequate provision for nationwide implementation of the regulatory framework, subsequent to the successful completion of the consultative period?				
5.8	Is the proposed approach for regulating laboratory biosafety and biosecurity accompanied by adequate public information and participation?				

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5.9	Does the implementation programme include:				
5.9.1	• An effective inspection system and programme for monitoring the implementation process?				
5.9.2	• An effective inspection system for the surveillance of compliance with the regulatory requirements?				
Enforcement					
5.10	Which institution is responsible for the development of the inspection and monitoring system? **Note:** It is generally recommended that the NBBC or the NRA take the lead role in order to promote acceptance of the NBBF.	X			
5.11	Do the regulatory authorities which have responsibility for inspection and monitoring activities have enough adequately educated and trained staff who are able to carry the necessary inspections?				

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5.12	Are the inspection and assessment functions exclusively performed by governmental authorities in the country?				
5.13	If the answer to Q5.12 is no and inspection and assessment functions are NOT exclusively performed by governmental authorities, what alternative or supplementary approaches to enforcement and inspection are employed? **Note:** Alternative approaches might include the use of peer evaluation systems (which rely on the recruitment of adequately trained assessors from for example, the professional biomedical laboratories).				

STEP 6
Establish national information exchange networks and international partnerships

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
		Response (code as 1, 2, 3 or 4)	Reference (list any relevant supporting documents, reports or records)	Response (provide answer to open question(s) and/ or any additional information, as appropriate)	Response (code as 1, 2, 3 or 4)
6.1	Does the national regulatory body, ideally under the lead of the NBBC, develop and initiate efficient mechanisms of information exchange between all stakeholders?				
6.2	Is there functional information exchange between the various regulatory agencies and bodies with responsibilities for biosafety and biosecurity?				
6.3	Has the country taken steps to establish international partnerships to help support the development of its NBBF?				
6.4	Does international networking and collaboration support appropriate national actions with regard to:				
6.4.1	• comprehensive training programmes?				
6.4.2	• adequate surveillance concepts?				
6.4.3	• development of diagnostic services for identifying of new and emerging markers of biological risk?				

STEP 7
Review performance and adaptability to the national context and evolving risks

Item No.	Question	SELF ASSESSMENT	FOR SELF ASSESSMENT and EXTERNAL REVIEW USE		EXTERNAL REVIEW
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7.1	Is the NBBF evaluated periodically in order to assess its performance and verify that it has achieved the intended impact? **Note:** Various regulatory triggers, such as technological innovations, new and emerging biological agents and hazards and/ or international convention requirements, may also induce a review of the NBBF, over and above a standard, routine performance review that is referred to above.				
7.2	Is there an agreed timeframe for carrying out a routine performance review of the entire NBBF?				
7.3	Is there an agreed mechanism or procedure for carrying out a routine performance review of the entire NBBF?				
7.4	Is the NBBC involved in the planning and the conduct of a routine performance review of the NBBF?				

Notes

World Health Organization