WHO/HSE/GAR/BDP/2010.2

Responsible life sciences research for global health security

A GUIDANCE DOCUMENT

World Health Organization

Acronyms

BSL	Biosafety level
BWC	Biological and Toxin Weapons Convention
BBSRC	Biotechnology and Biological Sciences Research Council (United Kingdom)
CDC	Centers for Disease Control and Prevention of the Department of Health and Human Services (United States of America)
CSE	Council of Science Editors
EC	European Commission of the European Union
GMO	Genetically modified organism
IAP	InterAcademy Panel
ICLS	International Council for the Life Sciences
ICSU	International Council for Science
IHR	International Health Regulations
IUBMB	International Union of Biochemistry and Molecular Biology
IUMS	International Union of Microbiological Societies
HRS	Health research systems
MRC	Medical Research Council (United Kingdom)
NGO	Nongovernmental organization
NIH	National Institutes of Health of the Department of Health and Human Services (United States of America)
NRC	National Research Council of the National Academies (United States of America)
NSABB	National Science Advisory Board for Biosecurity (United States of America)
PHEIC	Public Health Emergencies of International Concern
rDNA	Recombinant DNA
RS	Royal Society of the United Kingdom
VBM	Valuable biological materials
WAME	World Association of Medical Editors
WHA	World Health Assembly of the World Health Organization
WHO	World Health Organization

Definitions

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

Bioethics The study of the ethical and moral implications of biological discoveries, biomedical advances and their applications, as in the fields of genetic engineering and drug research (*1*).[1]

Biological laboratory A facility within which biological agents, their components or their derivatives, and toxins are collected, handled and/or stored. Biological laboratories include clinical laboratories, diagnostic facilities, regional and national reference centres, public health laboratories, research centres (academic, pharmaceutical, environmental, etc.) and production facilities (the manufacturing of vaccines, pharmaceuticals, large-scale genetically modified organisms, etc.) for human, veterinary and agricultural purposes (*1*).

Biorisk The risk (risk is a function of likelihood and consequences) that a particular biological event (in the context of this document: naturally occurring diseases, accidents, unexpected discovery, or deliberate misuse of biological agents and toxins), which may affect adversely the health of human populations, may occur (*1*, *2*). An assessment of these risks can be both quantitative and qualitative.

Biorisk spectrum A continuum of biorisks ranging from naturally occurring diseases (chronic and infectious diseases), to accidents, to the deliberate misuse of biological agents and toxins with the intention to cause harm (**Figure 1**) (*2*).

Biorisk reduction The reduction of the occurrence of risks associated with exposure to biological agents and toxins, whatever their origin or source, encompassing the full spectrum of biorisks (*2*).

Laboratory biosafety The containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents and toxins, or their accidental release (*3*, *4*).

Laboratory biosecurity The protection, control and accountability for valuable biological materials[2] within laboratories, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release (*1*).

Dual-use life sciences research Knowledge and technologies generated by legitimate life sciences research that may be appropriated for illegitimate intentions and applications (*2*, *5*).

Life sciences All sciences that deal with organisms, including humans, animals and plants, and including but not limited to biology, biotechnology, genomics, proteomics, bioinformatics, pharmaceutical and biomedical research and techniques.

Global health security The activities required, both proactive and reactive, to minimize vulnerability to acute public health events that endanger the collective health of populations living across geographical regions and international boundaries (*6*).

---

[1] International Futures Program of the Organisation for Economic Co-operation and Development (OECD), Biosecurity oversight and codes (www.biosecuritycodes.org/gloss.htm, accessed October 2010).

[2] Valuable biological materials (VBM) are "Biological materials that require (according to their owners, users, custodians, caretakers or regulators) administrative oversight, control, accountability, and specific protective and monitoring measures in laboratories to protect their economic and historical (archival) value, and/or the population from their potential to cause harm. VBM may include pathogens and toxins, as well as non-pathogenic organisms, vaccine strains, foods, genetically modified organisms (GMOs), cell components, genetic elements, and extraterrestrial samples." (*1*)

Health research systems The people, institutions, and activities whose primary purpose in relation to research is to generate high-quality knowledge that can be used to promote, restore and/or maintain the health status of populations; it should include the mechanisms adopted to encourage the utilization of research (*7*).

Public health The science and art of preventing disease, prolonging life, and promoting health through the organized efforts and informed choices of society, organizations, public and private, communities and individuals (*8*). Health is defined by the Constitution of the World Health Organization as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.

Research excellence Research that is of high quality, ethical, rigorous, original and innovative.

Executive summary

Advances in life sciences research are inextricably linked to improvements in human, plant and animal health. Promotion of excellent, high-quality life sciences research that is conducted responsibly, safely and securely can foster global health security and contribute to economic development, evidence-informed policy making, public trust and confidence in science. Yet opportunities may also be accompanied by risks that need to be acknowledged and addressed. The risks under consideration in this guidance are those associated with accidents, with research that may pose unexpected risks and with the potential deliberate misuse of life sciences research. The opportunities offered by the life sciences are too important for governments and the scientific community (including individual researchers, laboratory managers, research institutions, professional associations, etc.) to leave the attendant risks unaddressed.

The purpose of this guidance is to inform Member States about the risks posed by accidents or the potential deliberate misuse of life sciences research and to propose measures to minimize these risks within the context of promoting and harnessing the power of the life sciences to improve health for all people. Although the issues addressed in this document can potentially interest a quite large audience, the proposed measures and the self-assessment questionnaire are of a public health nature. Health researchers, laboratory managers and research institutions are therefore the primary audience of this guidance.

There is no single solution or system that will suit all countries, institutions or laboratories. Each country or institution that assesses the extent to which it has systems and practices in place to deal with the risks posed by accidents or the potential deliberate misuse of life sciences research will need to decide which measures are most appropriate and relevant according to their own national circumstances and contexts.

However, as recognized by the World Health Assembly in 2002 (Resolution WHA55.16), one of the most effective ways to prepare for deliberately caused disease is to strengthen public health measures for naturally occurring and accidentally occurring diseases. This guidance contributes to the implementation of WHA55.16 and promotes a culture of scientific integrity and excellence, distinguished by openness, honesty, accountability and responsibility. Such a culture is the best protection against the possibility of accidents and deliberate misuse, and the best guarantee of scientific progress and development.

Moreover, countries and institutions may consider drawing on the biorisk management framework for responsible life sciences research developed by this guidance. This integrated framework rests on three pillars supporting public health.

- **Research excellence** – this concerns fostering quality in life sciences activities, which is the basis for developing new treatments and therapeutics, strengthening health research systems, and promoting public health surveillance and response activities. These elements are essential to protecting and improving the health and well-being of all people.

  As such, countries and institutions are invited to:

  — Support capacity development for research as this is essential for reducing health inequalities and for ensuring the proper use of life sciences;
  — Use existing tools and frameworks, such as health research systems (HRS), the WHO strategy on research for health and the International Health Regulations (IHR) as these can provide useful tools for contributing to responsible life sciences research.

- **Ethics** – this involves the promotion of responsible and good research practices, the provision of tools and practices to scientists and institutions that allow them to discuss, analyse and resolve in an open atmosphere the potential dilemmas they may face in their research, including those related to the possibility of accidents or misuse of the life sciences.

  As such, countries and institutions are invited to:

  — Use existing ethical platforms, if appropriate;
  — Promote ethics education and training for students and professionals;
  — Encourage discussion and reflection on research practices;
  — Hold institutions and researchers to account and ensure they are aware of their responsibilities;
  — Ensure institutions and researchers are aware of existing and new legislation, regulations at the country but also at the regional and international levels.

- **Biosafety and laboratory biosecurity** – this concerns the implementation and strengthening of measures and procedures to: minimize the risk of worker exposure to pathogens and infections; protect the environment and the community; and protect, control and account for valuable biological materials (VBM) within laboratories, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release. Such measures reinforce good research practices and are aimed at ensuring a safe and secure laboratory environment, thereby reducing any potential risks of accidents or deliberate misuse.

  As such, countries and institutions are invited to:

  — Conduct biosafety and laboratory biosecurity risk assessments and, based on these, apply appropriate risk reduction measures;
  — Implement a laboratory biorisk management system;
  — Explore the use of existing biorisk management structures (e.g. laboratory biorisk management adviser and the biosafety committee) to address issues related to the risks posed by life sciences research;
  — Set performance objectives and work on continuous improvement.

A culture of responsible life sciences practice is most likely to result when the leadership within the organization supports and fosters such a management framework.

In implementing the above biorisk management framework for responsible life sciences research, countries and institutions are encouraged to consider:

— Reinforcing public health capacities in terms of research for health, biosafety and laboratory biosecurity management and ethics;
— Investing in training personnel (laboratory staff and researchers) and students in ethics, the responsible conduct of research, and biosafety and laboratory biosecurity.
— Ensuring compliance with biosafety and laboratory biosecurity;
— Seeing multi-stakeholder issues, with different layers of responsibilities and encourage coordination among stakeholders;
— Using existing mechanisms, procedures and systems and reinforce local institutional bodies (if they exist).

Another major component of this guidance is a self-assessment questionnaire, which is intended to help health researchers, laboratory managers, and research institutions identify and build on strengths and address weaknesses in each of the three pillars of the biorisk management framework. Going through this process will provide an assessment of the extent to which systems are in place in the national public health system and individual laboratories to address the risks of accidents and the potential deliberate misuse of science and to identify priority areas where action is necessary to ensure high-quality, safe, secure and responsible research practices across the life sciences.

In general, oversight, safety and public security should be pursued in a manner that maximizes scientific progress and preserves scientific freedom. Any controls over life sciences research need to be proportionate and risk-based, should not unduly hamper the development of the life sciences and should not discourage scientists from working with important pathogens. This requires excellent facilities, and the management of them (including laboratories), leadership with integrity, a robust ethical framework, training and capacity development, institutional development and regular review.

1. Introduction

1.1 Context, purpose, audience and scope of the guidance

1.1.1 Context

When the reconstruction of the 1918 influenza A (H1N1) pandemic virus, also known as the Spanish Flu virus, was published in 2005, many people considered it a remarkable achievement that could help combat future influenza pandemics. At the same time, it raised concerns that the resurrected virus might escape from laboratories (as happened with severe acute respiratory syndrome [SARS] coronavirus in 2003–2004) or that the knowledge gained from this research could be deliberately misused to cause harm. Research-related laboratory accidents have the potential to affect laboratory workers, the environment, and local and more distant communities. The 2001 anthrax letters in the United States of America, which killed five people and infected 22, had a worldwide impact and underscored the role of public health systems in responding to the deliberate misuse of a biological agent (*9*). Other kinds of research misuse that may be dangerous to public health and have a significant economic burden include deliberately neglecting or side-stepping good research practices and codes of conduct, which are meant to ensure standards of ethics, safety and quality (*10*, *11*).

The reconstruction of the 1918 influenza A (H1N1) pandemic virus is one of a few experiments in recent years that have grabbed the media's attention and led to calls for better management of the potential risks associated with accidents or the deliberate misuse of life sciences research. There is a wide recognition that there is no "one size fits all" management measure and that such measures may be issued by different stakeholders. The need to have clear guidelines about what researchers, publishers, funding bodies, governments and other actors are expected to do with research raising possible risks as well as the need to have guidelines to avoid measures that would go beyond what is appropriate, have been emphasized (*12–14*).

The role of WHO in this area has been underlined by several groups, including by the National Research Council of the US National Academies of Sciences in their 2004 seminal report on the subject "Biotechnology Research in an Age of Terrorism: Confronting the Dual-Use Dilemma, also called the "Fink report" (*15*). It has also been noted that WHO as an international organization with direct links to policy makers and having wide acceptance as an authority in preserving public health, is particularly equipped to promote responsible life sciences research. By emphasizing the public health perspective of dual-use issues, this guidance can achieve a broad acceptance of the need to raise awareness in this area and thus be better able to implement the objectives of promoting responsible life sciences research in general on a global level.

A scientific working group, which met in WHO in 2006 to discuss the risks and opportunities of life sciences research for global health security, also underlined the important role of WHO to lead, in coordination with other stakeholders and in line with its public health mandate, global efforts and help maintain effective policies that will maximize the benefits of public health research while minimizing the risks (*2*). Moreover, participants at a WHO workshop on responsible life sciences research also underscored the need to have a foundational document on this topic (see **Annex 3**). As this subject is being addressed by many stakeholders with different interests and agendas, this document provides a unique international public health perspective on this issue, which is important to complement with other policy measures. Such a perspective also provides a platform for discussion.

The importance of a public health perspective on this topic is important for several reasons. The life sciences have the potential to address a host of public health, agricultural and environmental

challenges, making them a key driver of economic growth and an important element of health innovation for developing, as well as for developed countries (*16–19*). It is widely perceived that advances in the life sciences will continue to be significant in this century and that the impact will be similar to that of the life and physical sciences in the 20th century (*20*).

Capacity development for research is necessary for ensuring the proper use of life sciences research and minimizing accidents and potential for deliberate misuse (*21*). Research on conditions affecting the health status of poor people along with access and delivery tools are crucially needed. Despite the substantial increase in funding for research and development (R&D) in developing countries (*22*) and the investment in life sciences R&D expertise by countries such as Brazil, China and India (*22*), only a small proportion of the quadrupling global investments in R&D since 1986 has been spent on diseases affecting poor people (*23*). Over the same time, health status has deteriorated in many developing countries,[1] which are increasingly suffering from the double burden of disease, combining the so-called diseases of poverty (infectious diseases and maternal, perinatal and nutrition conditions) with injuries and chronic noncommunicable diseases such as cancers, diabetes and cardiovascular diseases (*22, 24*).

It is well recognized that more needs to be done to reduce inequities in health conditions among populations, to bridge the technological gap between developed and developing countries (*16, 25*), and to translate new knowledge into health products. Access to biotechnologies therefore remains a major aspect for health development (*18*). The Millennium Development Goals have stressed the important role of the life sciences for human security. Biomedical research and emerging genomics techniques along with international collaboration and partnerships can help to achieve these and other development goals (*26*).

Yet opportunities are often accompanied by a number of risks. Advances in life sciences research and new biotechnologies such as genomics, synthetic biology, stem-cell research, and genetically modified organisms and foods have already raised a series of complex legal, social and ethical issues. In response, many countries have designed and implemented different regulatory frameworks that reflect their own political cultures, national priorities, local contexts and perceptions of risks (*27, 28*). The same country-based approach may be taken for the equally complex and challenging issues around the potential risks of accidents or the deliberate misuse of life sciences research.

The field of public health is concerned with protecting and promoting the health of communities and therefore must give due consideration to both the benefits and the possible risks of life sciences research for public health. At the same time, managing these risks may potentially harm public health if controls on research are so stringent that they stall advances in the life sciences and make international collaboration difficult (*2*). Any controls on life sciences research need, therefore, to be proportionate and balance risks and benefits.

Finding the right balance is essential for several reasons. First, control over research should not unduly hamper the development of the life sciences and should not impede access to biological materials and resources necessary to address public health challenges, including new infectious diseases. A situation that discourages scientists from working with important pathogens should be avoided. At the same time, increasing capacity for the life sciences should be accompanied by the promotion of responsible life sciences management.

Second, strong public confidence in life sciences research needs to be established and continuously nurtured. Research is essential for public health. Communication, international collaboration and openness, which are central to a public health perspective, are indispensable for global health security, scientific discovery and evidence-based measures.

Finally, information on this issue is uneven among Member States. Providing information on this topic to the various ministers of health in WHO Member States will:

- help them to rationally explain the issues to their constituencies and populations;
- help them to inform, educate and advise colleagues in other ministries;
- help them to plan rational and feasible emergency response plans should an adverse event occur;
- better equip them to assess what capabilities (and bioresources, e.g. exotic pathogens) existing within their own countries for the types of potentially dangerous research;
- should Member States be considering national regulations, understanding this issue will help

[1] By 2003, the number of people living in developing countries represented more than 80% of the total world population (*22*).

them formulate workable and effective guidelines and safeguards;
- understanding it will enable them to contribute better to global debate on the topic and, at the same time, bringing with them their own unique perspectives.

1.1.2 Purpose and audience

The purpose of this guidance is to inform Member States about the risks posed by accidents or the deliberate misuse of life sciences research and to propose measures to minimize them within the context of promoting and harnessing the power of the life sciences to improve health for all people. This guidance aims at strengthening the culture of scientific integrity and excellence characterized by openness, honesty, accountability and responsibility: such a culture is the best protection against accidents and deliberate misuse, and the best guarantee of scientific progress and development.

This guidance provides Member States with a conceptual framework for individual adaptation according to national circumstances, contexts, needs and capacities. Countries, research institutions, and laboratories are encouraged to review the proposed measures and to adapt them accordingly.

The issues addressed in this document can potentially interest a quite large audience: from policy-makers, relevant national regulatory authorities to scientific community (including researchers, laboratory scientists and managers, research institutions, professional associations, students, educators and journal editors).

However, the measures proposed under the biorisk management framework are of a public health nature and the self-assessment tool has been designed and field-tested within this framework and with the help of health researchers and laboratory managers. Health researchers, laboratory managers and research institutions are therefore the primary audience of this document, noting that the self-assessment questionnaire can be adapted to countries and institutions' needs.

Using this guidance will provide researchers and institutions with:

- a better understanding of the potential risks associated with accidents and the deliberate misuse of life sciences research;
- learn about practical measures that will enable them to manage some of the risks posed by life sciences research;
- assess their needs and capacities using a self-assessment tool to review existing structures and mechanisms and identify potential needs.

1.1.3 Scope of the guidance: WHA55.16 and the biorisk management framework for responsible life sciences research

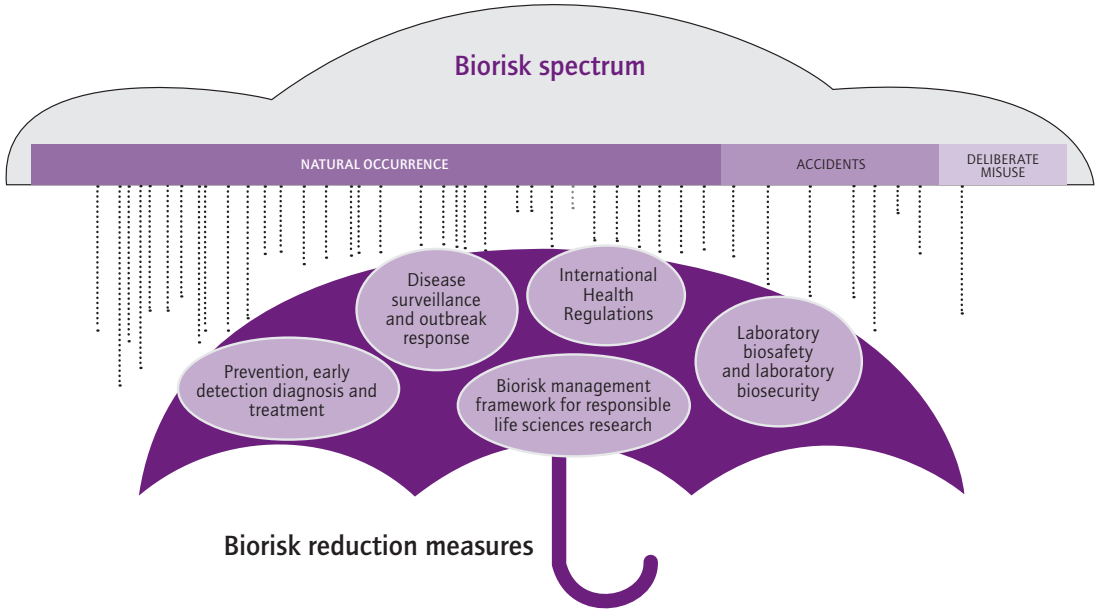
This document complements previous publications on the subject published by WHO (*2*, *5*, *29*) and links up with other areas of work of WHO, in particular, biosafety and laboratory biosecurity, ethics and some areas of work falling under research policy and cooperation. Compared to other documents and approaches published on this subject, the WHO approach is unique because it looks at this issue from a public health angle. As this is a multi-stakeholder issue, policy measures have been proposed by different sectors, including governments, security, academic and private sectors. This guidance, its biorisk framework and its self-assessment tool however only discuss measures based on and supporting public health. Moreover, this document looks at life sciences activities in general and does not focus on a particular field of life sciences. In addition, it takes a country-based approach, noting that over time, comparison and sharing of experiences and best practices of country and institutional approaches can be done at regional and global levels in order to support international cooperation and ensure that no incompatible measures are put forward.

The document and its approach are also to be understood within the context of the World Health Assembly in 2002 (Resolution WHA55.16). As recognized by resolution WHA55.16, one of the most effective ways to prepare for deliberately caused disease is to strengthen public health measures to address naturally occurring and accidentally occurring diseases. While recognizing the important role of other actors, such as the security[1] and academic communities, this guidance has a public health objective and the conceptual framework and measures proposed re-emphasize the WHA55.16 approach.

This guidance has also been developed within the wider context of the "biorisk spectrum" in that it advocates an all-encompassing risk management approach, in accordance with WHA55.16. The continuum of potential natural, accidental or deliberate exposure of humans, animals and/or plants to

[1] See the 1975 Biological Weapons Convention and the United Nations Security Council 1540.

Figure 1. The biorisk spectrum and biorisk reduction measures



pathogens or toxins likely to harm public health encompasses the full spectrum of biological risks to global health security (see **Figure 1**) (*2*). Such risks include, for instance, new infectious diseases such as the pandemic influenza A (H1N1) 2009 virus, avian influenza (H5N1) and severe acute respiratory syndrome (SARS), re-emerging diseases and modified strains of long-established diseases (e.g. multi- and extensively drug resistant tuberculosis), laboratory accidents, the unintended consequences of research, lack of awareness, negligence, and the deliberate misuse of life sciences research.

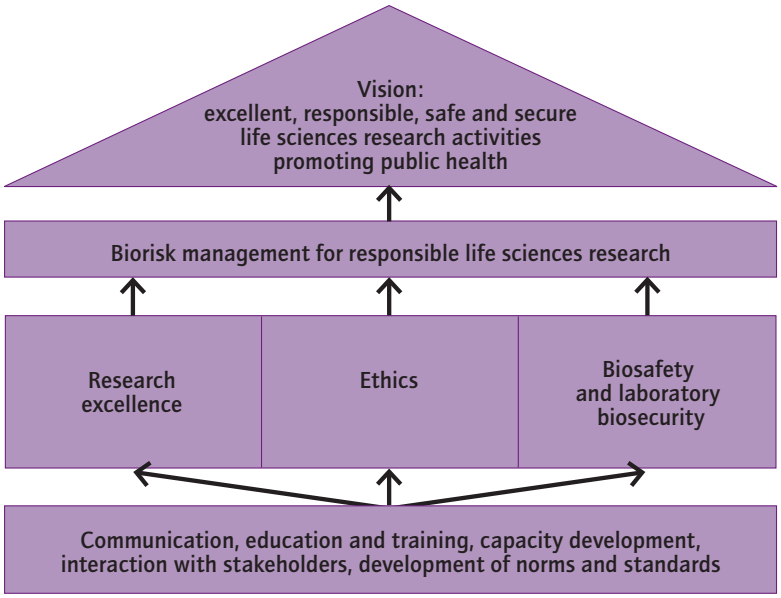
In this guidance, the term "biorisk reduction" is defined as the reduction of the occurrence of risks associated with exposure to biological agents and toxins, whatever their origin or source. Different levels of risk can be assigned across the biorisk spectrum, according to a country's situation or institutional contexts (*2*). Measures put forward using this approach will both help to address the consequences of naturally occurring diseases and reduce the likelihood of accidents or the deliberate misuse of life sciences research.

Responsible life sciences research that is conducted ethically by well-trained professionals in laboratories that have safety and security measures in place, constitutes one public health component of biorisk reduction. Other complementary public health measures that are an integral part of biorisk reduction, but which are not detailed in this guidance, include prevention, early detection, diagnosis and treatment of naturally occurring diseases, disease surveillance, preparedness and outbreak response, compliance with the International Health Regulations (2005),[1] and laboratory biorisk management through biosafety and laboratory biosecurity.

This guidance document focuses on one measure of biorisk reduction, namely the biorisk management framework for responsible life sciences research (see **Figure 2**). The framework focuses on a vision of promoting excellent, high-quality, responsible, safe and secure research, where the results of the research foster advancements in health, economic development, global health security, evidence-informed policy-making, and public trust in science. Underpinning this vision is the importance of managing risks posed by accidents and the deliberate misuse of life sciences research activities through an integrated approach that recommends investing in capacities in three pillars supporting public health: research excellence, ethics, and biosafety and laboratory biosecurity (each pillar is discussed in detail in **Section 3**). At the foundation are several cross-cutting elements: communication, education and training, capacity development, interaction with stakeholders (scientists, publishers and editors, ethicists, national academies of sciences, security communities, gov-

[1] For additional information on the International Health Regulations (http://www.who.int/ihr/en/, accessed October 2010). See also (*9*).

Figure 2. Biorisk management framework for responsible life sciences research



ernments and international organizations), and the development of norms and standards. A self-assessment questionnaire has also been developed and is presented in Section 4 to help countries and institutions assess their strengths and weaknesses and to support implementation of the biorisk management framework. The self-assessment questionnaire is not a tool to evaluate the adequacy of the measures developed by other sectors (security, academia, publishers and editors, etc.) but it recognizes the importance of collaboration between different sectors.

1.2 Methodology

A review of the available evidence of the risks and of the policies put forward to manage those risks (see Section 2) has been made by doing a literature review of a variety of different documents. These included peer reviewed journals, background documents, meeting reports, codes of conducts, laws, information shared at international meetings and provided by countries. Most of this information has been collected over the past four years and builds up on previous WHO publications.

Section 3 builds upon the evidence collected in Section 2 and develops a conceptual framework, which was has been presented and discussed at several international meetings. This framework recognizes that "one size does not fit all", and neither should it; that the uniqueness of countries and their specific needs should be identified and met, and that each country would have its own vision on where it wishes to go and how to get there. At the same time, it has to be understood, that in the national and global interest, certain essential standards of the pursuit of science and of scientific research need to be in place: these are the three pillars (research excellence, ethics and biosafety and laboratory biosecurity) and to help evaluating those essential standards, a self-assessment questionnaire has been developed in Section 4 of this guidance.

A first draft document was commented in April/May 2009 by the Guidelines review group. The Guidelines review group workshop on responsible life sciences research was held in Geneva, 22–24 June 2009 to review the content of the document and its implementation (Annexes 2 and 3). The workshop re-emphasizes the importance of the document and its approach. Sections of this guidance have also been reviewed internally with colleagues working on research policy, ethics and on biosafety and laboratory biosecurity (Annex 1).

After the tenure of the Guidelines review group workshop, comments were accommodated and the document was edited. This second draft was sent for peer review in December 2009/January 2010 (Annex 1).

A pilot test of the self-assessment questionnaire presented in Section 4 was conducted in October 2009 with a small group of scientists at the National Institute of Communicable Diseases (NICD), South Africa. It helped to strengthen and refine some of the questions and assess the type of information and results that could be expected from such a questionnaire. Additional pilot tests of the questionnaire will be performed, as appropriate.

As the issues raised in this document are evolving, modifications to this guidance will be made as additional evidence becomes available. This guidance will be reviewed two years after its publication.

1.2.1 Terminology

Although the use of the word "biosecurity" is increasing, no universally agreed definition has emerged. As is the case with biosafety, different sectors are using the same word with different

meanings, which in turn may lead to some confusion (*30–32*). Biosecurity was initially used in reference to animal and plant health;[1] more recently, it has been used by public health, academic (*33*), policy and security communities.[2] This guidance uses the WHO concept of "laboratory biosecurity", which is an extension and a complementary dimension of laboratory biosafety (*1*)[3] (see **Section 3.3**). In other words, by implementing good laboratory biosafety practices, laboratories are already implementing some of the requirements of laboratory biosecurity.

There is a similar lack of agreement around the concept of "dual-use research". Several definitions have been put forward, but there is no commonly agreed understanding as to what constitutes dual-use research.[4] Some also argue that the dual-use label is misleading and may cause confusion in regard to certain types of research that nevertheless need to be undertaken for public health. For the purpose of this guidance, dual-use research is understood as knowledge and technologies generated by legitimate life sciences research that may be appropriated for illegitimate intentions and applications. This working definition has to be understood within WHA55.16, whose language has the advantage of focusing more on the action and less on the definition.

This document will refer to the "potential risks posed by accidents or the deliberate misuse of life sciences research". In this guidance, the words "accidents" (or research accidents) reflects the fact that research activities may unexpectedly pose some risks via "accidental" discoveries (such as the mousepox experiment, see **Box 1**). Under this approach, dual-use research can both be associated with "accidents" and risks caused by "deliberate" misuse. This guidance is not specifically concerned with "laboratory accidents", as this important area of work is already being covered by the WHO laboratory biosafety manual (*3*).

1.3 Structure of the guidance

This document is organized into four sections. This section provides an overview of the guidance, describing the context, purpose, audience, scope and methodology.

Section 2 reviews cases of life sciences research that have raised concerns over the past few years and examines the policy options that have been put forward by different stakeholders to address these concerns.

Building on this, **Section 3** describes the three pillars of the guidance's biorisk management framework for responsible life sciences research: research excellence, ethics, and biosafety and laboratory biosecurity. It also shows how the pillars respond to several key issues raised in **Section 2** and how investing in these areas is complementary and self-reinforcing for public health.

Section 4 presents the main steps for carrying out a self-assessment of national and institutional biorisk management capacity. It includes a questionnaire, which assesses elements of the three pillars, and can be used to inform a tailored approach to implementing the biorisk management framework, adapted to each country's circumstances and needs.

[1] For animal health, biosecurity refers to good hygiene practices that help prevent the emergence and spread of animal diseases. For plant health, biosecurity refers to controls to protect plants against different types of pests but also against animals or practices that could have adverse effects on plants. The Food and Agriculture Organization (FAO) considers biosecurity to be a "strategic and integrated approach that encompasses the policy and regulatory frameworks (including instruments and activities) that analyse and manage risks in the sectors of food safety, animal life and health, and plant life and health, including associated environmental risk." Biosecurity for agriculture and food production (http://www.fao.org/biosecurity/, accessed October 2010), (http://www.fao.org/ag/agn/agns/meetings_consultations_2003_en.asp,accessed October 2010) and (*34*).

[2] States Parties to the Biological Weapons Convention have also noted their common understanding on "biosafety "and "biosecurity" within the context of the Convention (*35*).

[3] The Organisation for Economic Co-operation and Development (OECD) has also developed best practices guidelines for their Biological Resources Centres (BRCs). OECD refers to biosecurity as the "institutional and personal security measures and procedures designed to prevent the loss, theft, misuse, diversion or intentional release of pathogens, or parts of them, and toxin-producing organisms, as well as such toxins that are held, transferred and/or supplied by BRCs". While the OECD and WHO definitions are relatively similar, they differ in their approach because the OECD does not link laboratory biosafety to laboratory biosecurity measures (*36*).

[4] For definitions of dual use, see for instance (*5*, *15*, *37*).