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SHARP

Strengthened International HeAlth Regulations & Preparedness in the EU

Deliverable 7.3 for Joint Action SHARP

Recommendations for risk management - a Guidance Tool for Enhancing Biorisk Management in European Laboratories (EBRM-Guidance Tool)

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Guidance Tool for Enhancing Biorisk Management in European Laboratories (EBRM-Guidance Tool)

Tuija Koivula and Åsa Szekely Björndal, Unit for Biopreparedness, Department for Microbiology, Public Health Agency of Sweden (PHAS).

Background

This document is intended to serve as a guidance tool for enhancing biorisk management in European containment laboratories. The EBRM-Guidance Tool, hereinafter referred to as the Guiding Tool, contains a wide-ranging collection of information to be utilised when establishing or maintaining a laboratory biorisk management system. Such a system is pivotal for laboratory activities that involves various sorts of handling of biological material including transport, transfer and storage of materials that may contain infectious agents. Since the document was drafted within Work Package 7 of the Joint Action SHARP project, the attended use of the Guidance Tool is laboratories handling highly infectious agents in risk group 3 and 4. The information in the Guidance Tool focuses on essential legislation and provides qualitative guidance that may have an impact on managing biological hazards and threats in facilities handling and storing infectious agents.

In 2018 a need for improvement and consolidation of biorisk management in SHARP partner laboratories was identified in the EU Agreement of the SHARP Joint Action. Already in 2015, the Integrated European Checklist for Laboratory Biorisk Management in Handling of High Consequence Risk Group 3 and 4 Agents ”ECL-Biorisk” was developed within the project Quality Assurance Exercises and Networking on the Detection of Highly Infectious Pathogens, QUANDHIP. The ECL-Biorisk checklist is regularly used by SHARP partners for self-assessment of detailed technical aspects of barrier protection at the laboratory level. The Guidance Tool, on the other hand, provides examples of a number of check-lists, guidances, standards and other documents that can be used to respond to the requirements set at the organisational and laboratory level. With a broader perspective beyond the more technical aspects on the laboratory level, the Guidance Tool can be used complementary to ECL-Biorisk checklist. The Guidance Tool is intended to be used by laboratories within the SHARP consortium in order to enhance a systematic approach to laboratory biorisk management.

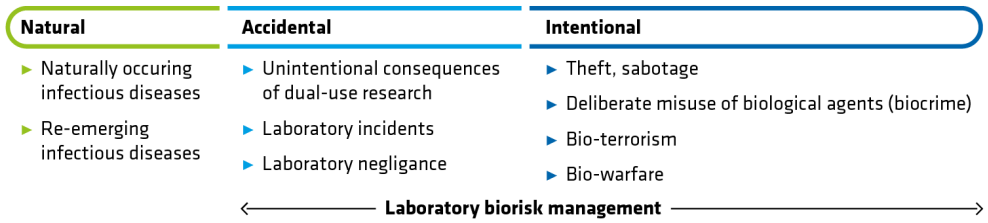
Content

What is laboratory biorisk management?

Biorisk management is defined as coordinated activities to direct and control an organisation, in our case a laboratory, with regard to biological risk or "biorisk". These activities include both administrative controls as well as laboratory procedures and practices.

Biological risks in the laboratory setting can appear in a wide spectrum, from normal events with naturally occurring infectious diseases and their laboratory diagnostics to unintentional consequences of handling biological agents leading to laboratory incidents or accidents. Biological risks may also appear from to events of unintentional release during research, through laboratory negligence, leading to laboratory-associated infection (LAI). In extremely rare cases, biological agents are also a source of risk for malicious intent through deliberate misuse and acts of crime and terrorism (Figure 1).

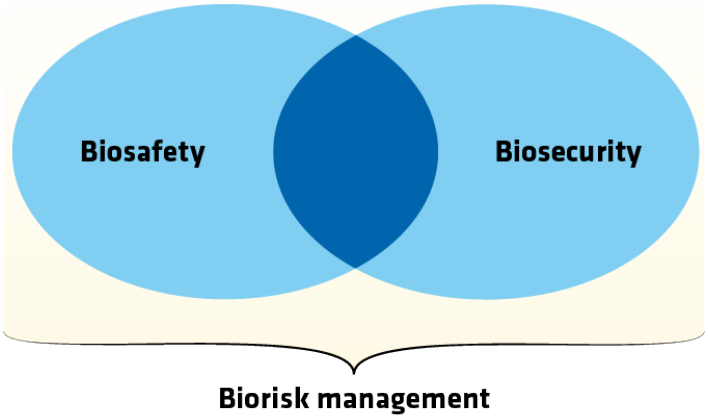
Figure 1. The spectrum of biological risks.



Organisations that have implemented an effective programme for biorisk management contribute to the reduction of threat to society posed by infectious biological agents in that the risk for unintentional release or malicious use is significantly reduced.

The Guidance Tool covers both biosafety and biosecurity aspects of laboratory biorisk management. Although there is an overlap between biosafety and biosecurity (Figure 2), the two parts include significant differences as described further down in the text.

Figure 2. Laboratory biorisk management includes biosafety and biosecurity.



To define biosafety, we have chosen the WHO definition (WHO Laboratory biorisk management, 4th edition, 2020). Biosafety is a discipline that includes containment principles, technologies and practices to prevent unintentional exposure to biological agents or their inadvertent release. Biosafety measures include for instance good microbiological practices, containment devices, personal protective equipment, decontamination principles and waste management.

Risk assessment is pivotal and should be performed before handling infections biological materials. The risk management process starts with hazard identification and once a hazard has been identified as a potential risk, an assessment is performed taking work procedures and work environment into the equation. Based on the results from the risk assessment, measures will be taken to eliminate or mitigate the biological risk. If not eliminated, which rarely happens, control measures, including specific biosafety measures ensure that the risk is tolerated and reduced to an acceptable level.

For the term biosecurity the WHO definition is also used (WHO Laboratory biorisk management, 4th edition, 2020). Biosecurity aims to prevent unauthorized access, loss, theft, misuse, diversion or release of biological agents. Biosecurity includes 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. Biosecurity measures include for instance codes of conduct, restricted access, locked freezers, camera surveillance and information security as some examples. Risk assessment with regard to biosecurity measures may include assessment of security threats and lead to the implementation of adequate biosecurity measures proportionate to the risk identified.

The SHARP framework for biorisk management

In order to strengthen the implementation of international regulations for workers protection (biosafety) and biosecurity when handling infectious biological agents, we recommend the documents in Table 1 to be considered as a minimum set of regulations and guidelines to be addressed by SHARP partners. The four listed documents include an essential EU-directive on workers protection, the international ISO-standard for laboratory biorisk management, the WHO guideline on laboratory biosafety and a laboratory check-list on requirement for BSL3 and BSL4 laboratories, developed by the previously EU-funded project QUANDHIP.

The framework documents in Table 1 can be found, among many other documents, in the Guidance Tool. The remaining documents of the Guidance Tool will assist organisations in their internal process to reach compliance to the recommended biorisk management framework. Although this framework has been developed within the SHARP project, it can also be advantageously addressed beyond this project, for instance by partner of the EMERGE laboratory network.

Table 1. A recommended framework for biorisk management. That includes a minimum set of standards and guidance to be addressed by SHARP partners.

Regulation or guidance that covers biorisk management	**Rationale for recommendation**
EU Directive on the protection of workers from risks related to exposure to biological agents at work (2000/54/EC) Year: 2000 Directive 2000/54/EC	Binding for all EU member states on minimum requirements for the health and safety of workers exposed to biological agents at work. The directive must be incorporated in national regulations in each member state and should be followed by all SHARP partners.
Integrated European Checklist for Laboratory Biorisk Management in Handling of High Consequence Risk Group 3 and 4 Agents (ECL-Biorisk) Year: 2015 ECL-Biorisk	Check-list for self-evaluation of a set of requirements for operating BSL3 and BSL4 laboratories. The check-list, created by the EU funded Joint Action QUANDHIP, was designed to guide the implementation of a biorisk management practices associated with the design and routine operation of high containment laboratories. The use of ECL-Biorisk is used to enable collaboration between SHARP partners. The ECL-Biorisk check-list is presently housed by the EMERGE network.
ISO 35001 Biorisk management for laboratories and other related organisations Year: 2019 ISO 35001:2019 Biorisk management	International standard for implementing a biorisk management system for all laboratory settings, including BSL2, BSL3 and BSL4. Complementary to the ECL-Biorisk, the ISO-standard puts additional focus on areas such as role and responsibilities of leadership and personnel reliability measures. The standard may be used by SHARP partners upon establishing and/or maintaining a biorisk management system on the organisational level.
WHO Laboratory biosafety manual 4th edition (LMB4) Year: 2020 WHO LBM4	International guidance that endorses a systematic, evidence-based assessment of the risks when working with biological agents in all kind of laboratory settings. LBM4 may be used by SHARP partners for adapting safety measures to any given work situation, including stationary laboratories and laboratory work performed under rural or mobile conditions.

Glossary of terms

Audit

Systematic, independent, and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled.

Reference: International standard ISO 35001:2019, 1st edition 2019-11

Biological agent

Any microbiological entity, cellular or non-cellular, naturally occurring or engineered, capable of replication or of transferring genetic material that may be able to provoke infection, allergy, toxicity or other adverse effects in humans, animals, or plants.

Reference: International standard ISO 35001:2019, 1st edition 2019-11

Biorisk

Effect of uncertainty expressed by the combination of the consequences of an event (including changes in circumstances) and the associated “likelihood” of occurrence, where biological material is the source of harm.

Reference: International standard ISO 35001:2019, 1st edition 2019-11

Certification

A third-party testimony based on a structured assessment and formal documentation confirming that a system, person or piece of equipment conforms to specified requirements, for example, to a certain standard.

Reference: WHO Laboratory biosafety manual, 4th edition (2020) and associated monographs

Containment

The combination of physical design parameters and operational practices that protect personnel, the immediate work environment and the community from exposure to biological agents.

Reference: WHO Laboratory biosafety manual, 4th edition (2020) and associated monographs

Facility

Operational unit and associated buildings and equipment used to manage biological materials.

Reference: International standard ISO 35001:2019, 1st edition 2019-11

Laboratory-associated infection (LAI)

Any infection acquired or reasonably assumed as a result of exposure to a biological agent in the course of laboratory-related activities. A person-to-person

transmission following the incident may result in linked secondary cases. Laboratory-associated infections are also known as laboratory-acquired infections.
Reference: WHO Laboratory biosafety manual, 4th edition (2020) and associated monographs.

Laboratory biosafety

Containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents or their inadvertent release.
Reference: WHO Laboratory biosafety manual, 4th edition (2020) and associated monographs

Laboratory biosecurity

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. Biosecurity aims to prevent their unauthorized access, loss, theft, misuse, diversion or release.
Reference: WHO Laboratory biosafety manual, 4th edition (2020) and associated monographs

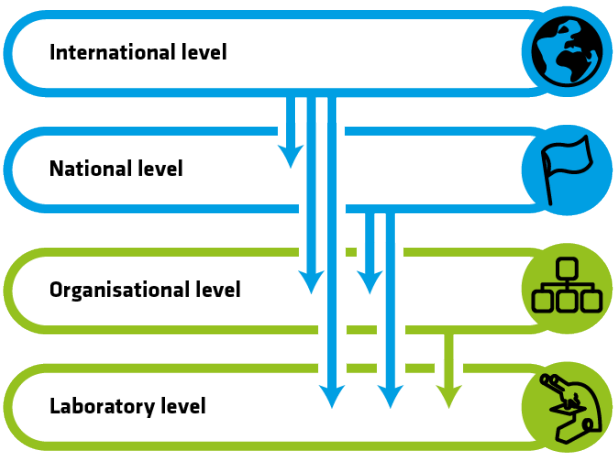
Laboratory biorisk management

Coordinated activities to direct and control an organisation with regard to biorisk.
Reference: International standard ISO 35001:2019, 1st edition 2019-11

How can the Guidance Tool be used?

Biorisk management systems are multi-layered in that they are based on international (global) as well as national, organisational and local laboratory requirements. The Guidance Tool is a managing resource that provides information to be used when setting up or assessing biorisk management within a laboratory. When utilising the Guidance Tool, the user is encouraged to explore a wide range of biorisk management requirements that goes beyond the basics for workers protection on a certain laboratory biosafety level as it also focusses on the need for biosecurity measures. In this Guidance Tool, "level" means a structural stage that calls for compliance to regulations or awareness of guidelines of best practise (Figure 3).

Figure 3. The Guidance Tool provides comprehensive information on regulation and guidelines.



Although daily laboratory activities addresses local policies and standard operating procedures of the individual organisation, this Guidance Tool is partly based on requirements and best practice at national and international level. As an example, for workers protection a set of international and national regulations needs to be followed when handling infectious biological agents. In addition, the organisation, as well as the individual laboratory, has usually developed its set of local rules that needs to be followed. These local set of rules can be based on international guidelines and best practise.

In the Guidance Tool, we are aiming at creating an awareness of managing biorisk with these four levels in mind. Each level includes brief descriptions and links to either regulatory or guiding documents. Some of the resources that are listed are for instance, standard requirements of a biorisk management system approach at the organisational level, while others provide more details on specific objectives at the laboratory level. Some of the documents that the Guidence Tool links to provides the user with possibilities to get an overview of overarching international demands on working safely and securely with high consequence pathogens, while other

documents includes details on technical specification, procedures and practices that should be at place at the laboratory level.

The Guidance Tool can be useful for self-assessment when evaluating the biorisk management programme in place within the organisation and for internal planning of new or existing laboratory activities. In addition, the Guidance Tool can support organisations in case of review, auditing and other undertakings, which aim to monitor and evaluate biorisk management.

The awareness check-list in Annex 1 includes all collected resources provided in the Guidance Tool and offers a way of actively documenting and gathering examples of successful implementation of requirements for biorisk management. Using the check-list also offers a way of documenting need for further improvement in relevant areas.

International level and National level

Target groups
Decision-makers, policy-makers and experts in for example government structures, regulatory authorities, expert authorities, microbiological laboratories and other related organisations.

Resources provided
Regulations, international agreements and guidances.

Implementation of regulations and guidance for safe handling of infectious agents enable collaboration between laboratories and other relevant organisations worldwide, which in turn may strengthen global health security.

International regulations covering biorisk management are legally binding documents based on international agreements to prepare for and protect against health threats posed by biological agents. Some of the most relevant regulators and other parties for European laboratories are the World Health Organization (WHO), United Nations (UN) and the European Commission (EC).

National laws and provisions are binding documents for organisations harbouring microbiological laboratories. To a great extent national laws, provisions and policies in place are based on international regulations and guidance documents.

The Guidance Tool does not aim to include national regulations from the consortium of Members States. Such information may be found at national regulatory authorities for workers' protection, occupational health and authorities responsible for handling, including storage and transport of biological material. National regulations and guidance could also be found at Research Councils or Committees.

The list below covers the following areas:

- International health security
- Workers' protection including work with genetically modified microorganisms (GMM) and transport
- Biosecurity
- CBRN and list of high consequence pathogens
- Dual-use research

Regulations

Regulations include examples of binding legislation, international agreements and treaties.

International health security, workers protection including work with GMM and transport

WHO – International Health Regulations (2005)

The International Health Regulations (IHR) are a legally binding instrument of international law signed by 196 countries. IHR require that all countries have the ability to detect, assess, report and respond to public health events, thereby protecting and securing global health.

International Health Regulations (2005)

EU – Regulation on serious cross-border health threats (2022/2371)

This legislative act provides the structures for coordinating responses to serious cross-border health threats within the EU.

EU regulation on serious cross-border threats to health (2022/2371)

International – Global Health Security Agenda: Action Packages (2014)

The Global Health Security Agenda (GHSA) is an effort by nations, international organisations, and civil society to accelerate progress towards a world safe and secure from infectious disease threats. In order to encourage progress towards these goals, the "Action Packages" concept was developed to facilitate regional and global collaboration towards specific GHSA objectives and targets.

Note: The GHSA Action Package dedicated to biosafety and biosecurity and can be found in the GHSA Biosafety and Biosecurity Action Package.

Global Health Security Agenda: Action Packages (2014)

UN – Cartagena Protocol on Biosafety (2003)

The Cartagena Protocol on Biosafety to the Convention on Biological Diversity is an international agreement which aims to ensure the safe handling, transport and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on biological diversity, taking also into account risks to human health.

Cartagena Protocol on Biosafety to the Convention on Biological Diversity (2003)

UN – Security Council Resolution 1540 (2004)

The Resolution requires all Member States to adopt and enforce appropriate laws and other effective measures to prevent the proliferation of nuclear, chemical or biological weapons and their means of delivery, in particular for terrorist purposes.

UN Security Council resolution 1540 (2004)

UN – The Biological Weapons Convention (BWC) (1975)

The first multilateral disarmament agreement, the Biological and Toxin Weapons Convention, banning an entire category of biological weapons. The Convention

covers the prohibition of the development, production and stockpiling of biological and toxin weapons and their destruction.

The Biological Weapons Convention (BWC) effectively prohibits the development, production, acquisition, transfer, stockpiling and use of biological and toxin weapons. It was the first multilateral disarmament agreement banning an entire category of weapons of mass destruction (WMD). The BWC is a key element in the international community's efforts to address WMD proliferation and it has established a strong norm against biological weapons.

Note: Acronym is Biological and Toxins Weapons Convention, BTWC.

The Biological Weapons Convention (BWC) (1975)

EU – Directive on the protection of workers from risks related to exposure to biological agents at work (2000/54/EC)

The Directive sets up minimum requirements for the health and safety of workers exposed to biological agents at work, and these are binding for all EU member states.

Note: Annex III includes a list of biological agents according to risk group (RG).

EU directive on the protection of workers from risks related to exposure to biological agents at work (2000/54/EC)

EU – Regulation on personal protective equipment (2016/425)

The Regulation on personal protective equipment (PPE) covers the design, manufacture and marketing of personal protective equipment**.** It defines legal obligations to ensure that PPE on the EU internal market provides the highest level of protection against risks.

EU regulation on personal protective equipment (2016/425)

EU – Directive on genetically modified micro-organisms (2009/41/EC)

The Directive lays down rules for the contained use of genetically modified micro-organisms (GMMs) for which containment/safety measures are used to limit their contact with the general population and the environment, in order to protect human health and the environment in the EU.

EU directive on genetically modified micro-organisms (2009/41/EC)

EU – Regulation on control of exports, brokering, technical assistance, transit and transfer of dual-use items (2021/821)

This list contains rules for the export of dual-use items including pathogens subjected to control of exports, brokering, technical assistance, transit and transfer. The main principle underlying this list concerns non-proliferation.

Note: Please see section 1C351 Human and animal pathogens and "toxins" for a complete list of agents.

EU regulation on control of exports, brokering, technical assistance, transit and transfer of dual-use items (2021/821)

UN – Recommendations on the Transport of Dangerous Goods (2019)

The Recommendations are addressed to governments and to the international organisations concerned with safety in the transport of dangerous goods and is applied worldwide for national or international transport by any mode. The Model Regulations cover general and special provisions, training and security, classification, dangerous goods list, packaging, consignment procedures (marking, labelling, placarding and documentation), requirements for the construction and testing of packaging, containers and tanks, etc.

Recommendations on the Transport of Dangerous Goods (2019)

UN – Agreement concerning the International Carriage of Dangerous Goods by Road (ADR)

This authoritative Agreement is intended to increase the safety of international transport of dangerous goods by road. Its Annexes A and B contain the technical requirements for road transport, i.e. the conditions under which dangerous goods, when authorized for transport, may be carried internationally, as well as uniform provisions concerning the construction and operation of vehicles carrying dangerous goods. They also establish international requirements and procedures for training and safety obligations of participants.

Agreement concerning the International Carriage of Dangerous Goods by Road (ADR) (updated every two years)

IATA – Dangerous Goods Regulations (DGR)

The IATA Dangerous Goods Regulations (DGR) manual is the global reference for shipping dangerous goods by air. The DGR covers all aspects of applicability, for example shipper and operator responsibilities, limitations concerning what is forbidden and hidden goods etc. Classification of dangerous goods to different categories like explosives, gases, flammable and multiple hazard material, packing instructions and packaging specifications for the different kinds of categories. Documentation needed like shipper's declaration, air waybill and handling covering storage, loading, inspection, information provision, reporting, training, document retention.

Dangerous Goods Regulations (DGR) (updated yearly)

Guidance

Documents posted here can be used as guidance to enhance a systematic approach to laboratory biorisk management in containment laboratories. The list below includes recognised guidance for working in the laboratory, examples of expert working groups in the field, manuals on selected high consequence pathogens and various lists of agents of concern/high consequence.

National biorisk management implementation guidance

WHO – Joint External Evaluation Tool (JEE-tool) 3rd edition (2022)

Technical framework in support to IHR (2005) monitoring and evaluation. A tool to assess country capacity to prevent, detect, and rapidly respond to public health threats independently of whether they are naturally occurring, deliberate or accidents. The purpose of the external evaluation is to measure country-specific status and progress in achieving the targets. Mission reports are available.

Note: Evaluation tool for the technical area Biosafety and biosecurity is found under the core area Prevent, page 44.

Joint External Evaluation Tool (JEE-tool) 3rd edition (2022)

EU – Biosafety-Europe Consortium Final Considerations (2008)

Biosafety-Europe was a coordination action funded through the 6th Framework Programme of the European Commission (EC), which aims to explore harmonization and exchange of biosafety and biosecurity practices within a pan-European network. The consortium comprises 18 partners from 10 European countries representing industry, academia and government agencies. Some recommendations Biosafety-Europe gives the relevant EC authority(s) are for example to develop and promote consensus based definitions of laboratory biosafety and laboratory biosecurity, to introduce risk-related laboratory biosecurity assessments alongside biosafety into already existing biosafety legislation, to require national authorities to collect and report data on laboratory acquired infections and to develop an EU–wide, evidence-based guidance on biosafety practices and procedures.

Biosafety-Europe consortium Final Considerations (2008)

Biosecurity

EU – European Biosecurity Regulators Forum (EBRF) (2020)

The European Biosecurity Regulators Forum (EBRF) is a European workgroup with the purpose to strengthen European biosecurity. The EBRF provides a forum for the sharing of knowledge and experience with regard to current human, animal and plant pathogen biosecurity and dual-use issues.

European Biosecurity Regulators Forum

OECD – Best practice guidelines on biosecurity for BRCS (2007)

This document contains the Best practice guidelines for biosecurity for biological resource centres (BRCs), provides support to governments in the recognition of BRCs, and describe the methods and protocols for secure maintenance and provision of biological material.

Note: The full set of recommendations, as well as background material and complementary guidelines can be found below in OECD Best practice guidelines for biological resource centres (2007).

OECD Best practice guidelines on biosecurity for BRCS (2007)

DK – An efficient and practical approach to biosecurity (2018)

The handbook was created by Denmark´s National Biosecurity Agency as an aid to those countries that are still in the process of fulfilling e.g. UN mandate UNSCR1540. The aim is to draw upon Denmark´s experiences with biosecurity to suggest an efficient and practical model that other countries can use, as a blueprint for establishing or improving their own biosecurity systems.

An efficient and practical approach to biosecurity (2018)

CBRN and lists of high consequence pathogens

EU – CBRN Action Plan (2010)

In 2010 the European Commission adopted its communication on strengthening chemical, biological, radiological and nuclear (CBRN) security in the European Union. The overall goal for the EU CBRN Action Plan is to reduce the threat and damage from CBRN incidents of accidental, natural and intentional origin. The Action Plan is broadly based on an all-hazard approach, including terrorist threats, and contributes to the implementation of the EU Counter Terrorism Strategy.

EU CBRN Action Plan (2010)

EU – List of high risk biological agents from EU CBRN Action Plan (2009)

Within the EU CBRN Action Plan a list of high risk biological pathogens to human animal and plats was established. The published list is for official use and to be shared with public and private stakeholders on a need-to-know basis only.

Note: The list can be found in Appendix I on page 16 in the EBRF-report on implementation of Action B2 of the CBRN Action.

Guidelines for the implementation of Action B2 - 2014

AU – The Australia Group (AG) (1985) and AG Biological agents list

The Australia Group (AG) is an informal forum of countries, which through the harmonization of export controls, seeks to ensure that exports do not contribute to the development of chemical or biological weapons. Coordination of national export control measures assists AG participants to fulfil their obligations under the

Chemical Weapons Convention and the Biological and Toxin Weapons Convention to the fullest extent possible. AG is administered by the Government of Australia.

Note: EU is a member of the Australia Group.

AU Government on Australia Group (1985)

The Australia Group Common Control Lists (2007)

Australia group biological agents list, updated on 28 February 2020

GB – The Approved List of biological agents (2021)

The Approved List is the list of classifications of biological agents approved by the Health and Safety Executive (HSE) for this purpose. Biological agents are bacteria, viruses, parasites and fungi which can cause harm to human health, usually due to infection (some are toxic or can cause an allergy). The Approved List is relevant to risk assessment for work with biological agents and the application of appropriate control measures.

The Approved List of biological agents (2021)

US – Select Agents and Toxins List (2021)

The biological agents and toxins on the list, by CDC and USDA Federal Select Agent Program, have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products.

Select Agents and Toxins List (2021)

US – CDC Bioterrorism Agents/Diseases, Category A-C (2018)

The United States public health system and primary healthcare providers must be prepared to address various biological agents, including pathogens that are rarely seen in the United States. High-priority agents (Category A) include organisms that pose a risk to national security. The second highest priority agents are listed in Category B and third highest priority agents (Category C) include emerging pathogens that could be engineered for mass dissemination in the future.

Bioterrorism Agents/Diseases, Category A-C (2018)

Dual-use research

WHO – Responsible life sciences research for global health security (2010)

The purpose of this guidance document 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.

Responsible life sciences research for global health security (2010)

US – Dual Use Research of Concern: A companion guide (2014)

A Companion Guide to the United States Government Policies for oversight of life sciences dual use research of concern. The guide provides tools for the identification, assessment, management, and responsible communication of dual-use research of concern.

Dual Use Research of Concern: A companion guide (2014)

Organisational level and Laboratory level

Target groups
Top management, laboratory management, biosafety professionals, laboratory supervisors, principal investigators, laboratorians.

Resources provided
General and technical guidances, standards and assessment tools.

Organisational top management needs to be committed by providing adequate resources, prioritising biosafety and biosecurity policies and integrating a biorisk management programme throughout the whole organisation. Such a programme could include a biorisk management system consistent with other management systems such as those for quality and competence in medical laboratories and occupational health and safety.

The biorisk management system should effectively enable an organisation to identify, assess, control and evaluate the biosafety and biosecurity risks. This includes documented policies and guidelines but also a quality assured system in place for documentation such as Standard operating procedures (SOPs) and regular assessments of established procedures to identify areas for improvements. The biorisk management system in place also needs to assure that workers receive appropriate education and training in biorisk management.

A biorisk management system in place at the organisational level enables personnel operating at the laboratory level to effectively manage activities on-site. Biorisk management at the laboratory level is comprehensive and includes detailed requirements on for instance personnel competence, handling of personal protective equipment, decontamination procedures, inactivation procedures for infectious specimens, routines for regular training of personnel, waste management, inventories of biological agents, transfer and shipment.

The list below covers the following areas:

- Laboratory manuals and guidance
- Risk management process
- Assessment and certification and
- Disease-specific guidance

Guidance

Documents posted here can be used as guidance to enhance a systematic approach to laboratory biorisk management in BSL3 and BSL4 laboratories.

Laboratory manuals and guidance

WHO – Laboratory biosafety manual 4th edition (LBM4) (2020)

This fourth edition of the LBM endorses a systematic, evidence-based and transparent assessment of the risks allowing safety measures to be balanced with the actual risk of working with biological agents on a case-by-case basis, in all kinds of laboratory settings.

The LBM4 suite consists of the core element (LBM4) and the following seven subject-specific monographs; Risk assessment, Laboratory design and maintenance, Biological safety cabinets and other primary containment devices, Personal protective equipment, Decontamination and waste management, Biosafety programme management and Outbreak preparedness and resilience. Associated monographs have been produced to provide more detailed information and help implement systems and strategies on specialized topics.

Note: LBM4 does not include information on risk groups of pathogens, nor biosafety levels of laboratories.

WHO Laboratory biosafety manual (LBM) 4th edition (2020)

WHO – Laboratory biosecurity guidance (2006)

This document provides detailed guidance on biosecurity within biological laboratories and addresses its basic principles and best practices.

Laboratory biosecurity guidance (2006)

SE – SIPRI Handbook of Applied Biosecurity for Life Science Laboratories (2009)

This handbook provides guidance and practical advice in applied biosecurity for personnel working with infectious pathogens and toxins that may affect the health of humans, animals and plants, ensuring secure handling and storage of biological materials.

Handbook of Applied Biosecurity for Life Science Laboratories (2009)

NL – Bureau Biosecurity Toolkits (web page)

The Biosecurity Office has developed various tools that can increase biosecurity awareness. The Biosecurity Self-scan Toolkit and the Vulnerability Scan are online tools to analyse biosecurity vulnerabilities in your organisation. The Dual-Use Quickscan is a tool with which can identify potential dual-use aspects in research. In addition, this tool contributes to stimulating dual-use awareness.

Note: At the website of the Office, the Code of Conduct for researchers on biosecurity can be found in Dutch. An English version of this document - A Code of Conduct for Biosecurity: Report by the Biosecurity Working Group - can however be found on the web page of project Biosecurity Central.

Bureau Biosecurity Toolkits

BE – Guidelines for researchers on dual use and misuse of research (2017)

This brochure is the result of a collaboration between the five Flemish universities (Belgium) within the ad hoc Working Group Dual Use of the Flemish Interuniversity Council, with active participation of Interuniversity Microelectronics Centre (Imec) and the Flanders Institute for Biotechnology (VIB). Institutions and funding bodies aim to raise researchers' awareness of the issues relating to dual use and misuse of research and help them to handle this appropriately. The brochure includes useful links to EC guidance documents.

Guidelines for researchers on dual use and misuse of research (2017)

WHO – Guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories - a stepwise approach (2020)

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

WHO Guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories - a stepwise approach (2020)

WHO – Laboratory leadership competency framework (2019)

The purpose of the framework is to outline the essential competencies needed by laboratory leaders to build and direct sustainable national laboratory systems for disease detection, control and prevention in health systems.

Laboratory leadership competency framework (2019)

GB – HSE Management and operation of microbiological containment laboratories (2019)

This guidance is issued by the Advisory Committee on Dangerous Pathogens, Health and Safety Executive (HSE) and is aimed at those responsible for managing, supervising, assessing and coordinating work in microbiological containment laboratories. One of the important aims of this guidance is to emphasize that it remains the duty holders' responsibility to manage the risks created from the work undertaken at their premises and should be used to make sure that any containment and control measures are suitable and sufficient to meet the minimum requirements.

Management and operation of microbiological containment laboratories (2019)

CA – Canadian Biosafety Handbook, 2nd edition (2016)

The handbook outlines information about the safe handling and storing of human and terrestrial animal pathogens and toxins in Canada and addresses concepts related to developing a comprehensive risk-based biosafety management program.

CA – Canadian Biosafety Handbook, 2nd edition (2016)

CA – Canadian Biosafety Guideline: Developing a Comprehensive Biosecurity Plan (2016)

The Canadian Biosafety Guidelines have been developed by the Public Health Agency of Canada (PHAC) and the Canadian Food Inspection Agency (CFIA) as an ongoing series of biosafety and biosecurity themed guidance documents. The guideline provides detailed guidance on the elements required for a biosecurity plan in Canadian facilities where pathogens and toxins are handled or stored.

Canadian Biosafety Guideline: Developing a Comprehensive Biosecurity Plan (2016)

US – Biosafety in Microbiological and Biomedical Laboratories, 6th edition (2020)

The Biosafety in Microbiological and Biomedical Laboratories (BMBL), a joint publication by the United States Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), has become the foundation of biosafety practice since it was first published in 1984. The core principle of this document is protocol-driven risk assessment and should be used as a tool in the assessment and proposed mitigation steps in biomedical and clinical laboratories.

Biosafety in Microbiological and Biomedical Laboratories 6th edition (2020)

US – Guiding Principles for Biosafety Governance: Ensuring Institutional Compliance with Biosafety, Biocontainment, and Laboratory Biosecurity Regulations and Guidelines (2017)

Given the importance of ensuring institutions have robust and comprehensive governance structures in place for the oversight of biosafety and biosecurity, the United States Government has developed the guidance document on biosafety and biosecurity governance. This document provides a number of guiding principles and best practices for ensuring institutions have appropriate organisational and governance structures in place to ensure compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines.

Guiding Principles for Biosafety Governance: Ensuring Institutional Compliance with Biosafety, Biocontainment, and Laboratory Biosecurity Regulations and Guidelines (2017)

US – A Biosafety Checklist: Developing a culture of biosafety (2015)

The checklist has been developed by Association of Public Health Laboratories (APHL) to serve as a starting point for laboratories to assess the biosafety measures that they have in place.

A Biosafety Checklist: Developing a culture of biosafety (2015)

WHO – Laboratory biosafety manual, 4th edition: Personnel protective equipment (2020)

The types of personnel protective equipment (PPE) worn in laboratories where biological agents are being handled are designed to protect the body, eyes and face, feet, hands and the respiratory system and hearing. This monograph provides information on the types, selection and use of PPE for personnel carrying out risk assessments, such as biosafety officers or laboratory managers, and laboratory personnel or scientists who use PPE for laboratory activities.

Personnel protective equipment (2020)

EU – ECDC technical document Safe use of personal protective equipment in the treatment of infectious diseases of high consequence (2014)

The scope of the tutorial is to improve the protection of staff dealing with infectious diseases of high consequence (IDHC). The document focuses on an extended set of personal protective equipment (PPE) components, which includes goggles, respirators, gloves, coveralls and footwear. The issues covered start with procurement and technical requirements as mandated by EU regulation, followed by critical aspects and known pitfalls in the donning (putting on) and doffing (removing) of PPE. At the same time, the tutorial encourages trainers and users to understand the rationales behind the different approaches.

ECDC technical document Safe use of PPE (2014)

CA – Pathogen Safety Data Sheets (web page)

Pathogen Safety Data Sheets (PSDSs) are technical documents that describe the hazardous properties of a human pathogens and provide recommendations for work involving these agents in a laboratory setting.

Note: This type of information may be readily available in several Member States. In for instance Sweden, PSDS are available in Swedish.

Pathogen Safety Data Sheets, Canada (regularly updated)

CA – Laboratory Biosafety and Biosecurity portal (web page)

The materials on this e-learning portal are provided to be used as part of a biosafety training program specific to your facility.

Note: E-learning material may be readily available in various Member States.

Laboratory Biosafety and Biosecurity portal, Canada (updated in April 2019)

Risk management process

WHO – Laboratory biosafety manual, 4th edition: Risk Assessment (2020)

The monograph on risk assessment describes the process of carrying out a risk assessment of work with a biological agent(s) so that an informed decision can be made by a laboratory facility about the risk control measures needed for the work

to be safely conducted. The targeted readership for the monograph is biosafety officers, laboratory personnel, laboratory managers and scientists who are performing the risk assessment.

Risk assessment (2020)

International – ISO 22367 Medical laboratories – Application of risk management to medical laboratories (2020)

This document specifies a process for a medical laboratory to identify and manage the risks to patients, laboratory workers and service providers that are associated with medical laboratory examinations. The process includes identifying, estimating, evaluating, controlling and monitoring the risks.

The requirements of this document are applicable to all aspects of the examinations and services of a medical laboratory, including the pre-examination and post-examination aspects, examinations, accurate transmission of test results into the electronic medical record and other technical and management processes.

ISO 22367:2020 Medical laboratories – Application of risk management to medical laboratories

International – ISO 31000 Risk management - Guidelines (2018)

The standard provides guidelines on managing risk faced by organisations and provides a common approach to managing any type of risk and is not industry or sector specific. The application of these guidelines can be customized to any organisation and its context and can be applied to any activity, including decision-making at all levels.

ISO 3100:2018 Risk management Guidelines

Assessment and certification

International – ISO 35001 Biorisk management for laboratories and other related organisations (2019)

The standard defines a process to identify, assess, control, and monitor the risks associated with hazardous biological materials and is applicable to any laboratory or other organisation that works with, stores, transports, and/or disposes of hazardous biological materials.

ISO 35001:2019 can be used as a tool in internal biosafety audits to identify deficiencies related to biosafety and biosecurity and provide guidance on how these deficiencies can be remedied.

Note: This ISO standard is the result of a global work with broad representation from government agencies, biosafety organisations, research institutes, the biotechnology industry and the EU. The original work was handled in a so-called CEN Workshop Agreement (CWA) and was named CWA 15793.

ISO 35001:2019 Biorisk management for laboratories and other related organisations

WHO – Laboratory Assessment Tool (2012)

The Laboratory Assessment Tool offers guidance to assess laboratories and national laboratory systems. The target audience is any stakeholder performing laboratory assessments: national health authorities, multilateral agencies, Non-Governmental Organizations (NGOs), laboratory managers, etc. This document describes a general process for assessing laboratories and provides two questionnaires to help assess national laboratory systems and individual laboratories.

Laboratory Assessment Tool (April 2012)

EU/EU-project – Integrated European Checklist for Laboratory Biorisk Management in Handling of High Consequence Risk Group 3 and 4 Agents (ECL-Biorisk) (2015)

This document was developed and agreed between 29 European BSL3-laboratories and 6 European BSL4-laboratories working together in the EU funded Joint Action "Quality Assurance Exercises and Networking on the Detection of Highly Infectious Pathogens" (QUANDHIP).

The checklist is designed to guide the implementation of a biorisk management system that ensures robust biosafety and biosecurity practices associated with the design, commissioning, routine operation and decommissioning of BLS3 and 4 laboratories. The developed document can be used as a tool for self-evaluation to assess current biorisk management systems.

Integrated European Checklist for Laboratory Biorisk Management in Handling of High Consequence Risk Group 3 and 4 Agents (ECL-Biorisk) (2015)

SE – Securing Biorisks (Säkra Biorisker) – self-assessment tool (2014)

This is a tool from Public Health Agency of Sweden for self-assessment to investigate to what extent an organisation has a system in place for managing biorisks. The tool is primarily used for self-control but can also be used for external auditing. The self-assessment tool follows the structure of the international agreement Laboratory biorisk management (CWA 15793).

Note: The CWA 15793 was further developed into the standard Biorisk management for laboratories and other related organisations, ISO 35001:2019. CWA 15793 can, however, still be accessed, free of charge, from for instance the International Federation of Biosafety Associations (IFBA). This Swedish self-assessment tool has however not been transformed into the new standard.

Securing Biorisks (Säkra Biorisker) – self-assessment tool (2014)

US – National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements (2006)

BSL-3 Laboratory Certification Checklist to be used in the US for certification of high containment high containment laboratories.

NIH – BSL3 Laboratory Certification Requirements (2006)

SG – National biosafety standards for maximum containment facilities (2019)

The document sets the requirements for facilities handling highly dangerous biological agents, which includes Second Schedule biological agents under the Biological Agents and Toxins Act (BATA) in Singapore. These biological agents are generally regarded as risk group 4 agents and pose a high risk to individuals as infections may lead to life-threatening diseases. The standard was published by the Ministry of Health Singapore.

National biosafety standards for maximum containment facilities (2019)

Disease-specific guidance

WHO – Tuberculosis laboratory biosafety manual (2012)

Following a technical consultation held between the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, in September 2008 an Expert Group was formed. The manual was developed from the Expert Group meeting and includes consensus on the basic principles of laboratory practices and design necessary to establish minimum criteria to ensure biosafety during TB microscopy, culture, drug-susceptibility testing (DST) and molecular testing in different countries and epidemiological settings.

This manual describes the minimum biosafety measures that should be implemented at the different levels of tuberculosis (TB) testing laboratories to reduce the risk of laboratory-acquired-infection.

Tuberculosis laboratory biosafety manual (2012)

WHO – Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance (28 January 2021)

The purpose of this document is to provide interim guidance on laboratory biosafety related to the SARS-CoV-2 virus to laboratories and stakeholders involved in COVID-19 laboratory work. This also includes the packaging and shipment requirements for sending specimens to WHO reference laboratories providing confirmatory and other testing for COVID-19.

Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance (28 January 2021)

WHO – WHO Global Action Plan for Poliovirus Containment (GAPIV) (2022)

This Biorisk Management Standard for Poliovirus-essential Facilities Holding Wild and/or Sabin/OPV Poliovirus Materials describes the international requirements for the facility safeguards established for two groups of PEFs: (1) laboratories handling and/or storing WPV/VDPV materials or Salk-inactivated polio vaccine (IPV) production facilities, and (2) laboratories handling and/or storing Sabin/OPV poliovirus materials or Sabin-IPV production facilities. The standard builds on the principles outlined in ISO35001: Biorisk management for laboratories and other related organisations, the principles of the WHO Laboratory Biosafety Manual, Fourth Edition and the extensive poliovirus scientific literature spanning nearly seven decades.

WHO Global Action Plan for Poliovirus Containment (GAPIV) (2022)

Annex 1. Awareness check-list

This check-list can be used for self-assessment to investigate to what extent your organisation is aware of various regulations and guidance in support of establishing and maintaining a biorisk management system. The recommended biorisk management framework, one regulation and three guidelines, to be addressed by SHARP partners, have also been indicated.

The Awareness check-list could, for instance, be used by an organisation that is planning to implement the international standard *ISO35001 Biorisk management for laboratories and other related organisations*. The ISO-standard on biorisk management focuses on the organisation's overall governance, strategy and planning, management, reporting processes, policies, values, and culture. Selected publications of the Guidance Tool may then be analysed and used to fill in the potential gap that may appear after internal review using the ISO-standard.

Another example is a public health organisation that plans to coordinate a national Joint External Evaluation (JEE) with regards to IHR. The Guidance Tool may then be used by the organisation to get an overview of to what extent national and international requirements for biosafety and biosecurity are met. The result can thus be used as a "prognostic marker" for moving forward in the process.

Awareness of Regulations on International Level and National Level NOTE: *, Specify selected choice in tick-boxes, e.g. relevance of publication to the individual organisation, suggested need for further exploration etc. **, Recommended biorisk management framework to be addressed by SHARP partners.	N/A	Yes	No	Not sure
WHO – International Health Regulations (IHR) (2005) Specification*:	☐	☐	☐	☐
EU – Regulation on serious cross-border threats to health (2022/2371) Specification*:	☐	☐	☐	☐
Global Health Security Agenda: Action Packages (2014) Specification*:	☐	☐	☐	☐
UN – Cartagena Protocol on Biosafety to the Convention on Biological Diversity (2003) Specification*:	☐	☐	☐	☐
UN – Security Council resolution 1540 (2004) Specification*:	☐	☐	☐	☐
UN – The Biological Weapons Convention (BWC) (1975) Specification*:	☐	☐	☐	☐
EU – Directive on the protection of workers from risks related to exposure to biological agents at work (2000/54) ** Specification*:	☐	☐	☐	☐
EU – Regulation on personal protective equipment (2016/425) Specification*:	☐	☐	☐	☐
EU – Directive on genetically modified micro-organisms (GMM) (2009/41/EC) Specification*:	☐	☐	☐	☐
EU – Regulation on control of exports, brokering, technical assistance, transit and transfer of dual-use items (2021/821) Specification*:	☐	☐	☐	☐
UN – Recommendations on the Transport of Dangerous Goods (2019) Specification*:	☐	☐	☐	☐
UN – Agreement concerning the International Carriage of Dangerous Goods by Road (ADR) Specification*:	☐	☐	☐	☐
IATA – Dangerous Goods Regulations (DGR) Specification*:	☐	☐	☐	☐
WHO – Joint External Evaluation Tool (JEE-tool) 3rd edition (2020) Specification*:	☐	☐	☐	☐
EU – Biosafety-Europe consortium Final Considerations (2008) Specification*:	☐	☐	☐	☐

EU – European Biosecurity Regulators Forum (2020) Specification*:	☐	☐	☐	☐
OECD – Best practice guidelines on biosecurity for BRCS (2007) Specification*:	☐	☐	☐	☐
DK – An efficient and practical approach to biosecurity (2018) Specification*:	☐	☐	☐	☐
EU – CBRN Action Plan (2010) Specification*:	☐	☐	☐	☐
EU – List of high risk biological agents from EU CBRN Action Plan (2009) Specification*:	☐	☐	☐	☐
AU – The Australia Group Common Control List (2007) Specification*:	☐	☐	☐	☐
AU – The Australia Group Biological Agents List (2020) Specification*:	☐	☐	☐	☐
GB – The approved list of biological agents (2021) Specification*:	☐	☐	☐	☐
US – Select Agents and Toxins List (2021) Specification*:	☐	☐	☐	☐
US – CDC Bioterrorism Agents/Diseases, Category A-C (2018) **Specification*:**	☐	☐	☐	☐
WHO – Responsible life sciences research for global health security (2010) **Specification*:**	☐	☐	☐	☐
US – Dual Use Research of Concern: A companion guide (2014) **Specification*:**	☐	☐	☐	☐

Additional information:

Awareness of Guidance on Organisational Level and Laboratory Level NOTE: *, Specify selected choice in tick-boxes, e.g. relevance of publication to the individual organisation, suggested need for further exploration etc. **, Recommended biorisk management framework to be addressed by SHARP partners.	**N/A**	**Yes**	**No**	**Not sure**
WHO – Laboratory biosafety manual (LBM) 4th edition (2020) ** Specification*:	☐	☐	☐	☐
WHO – Laboratory biosecurity guidance (2006) Specification*:	☐	☐	☐	☐
SE – SIPRI Handbook of Applied Biosecurity for Life Science Laboratories (2009) Specification*:	☐	☐	☐	☐
NL – Bureau Biosecurity Toolkits Specification*:	☐	☐	☐	☐
BE – Guidelines for researches on dual use and misuse of research (2017) Specification*:	☐	☐	☐	☐
WHO – Guidance on implementing regulatory requirements for biosafety and biosecurity in biomedical laboratories - a stepwise approach (2020) Specification*:	☐	☐	☐	☐
WHO – Laboratory leadership competency framework (2019) Specification*:	☐	☐	☐	☐
GB – HSE Management and operation of microbiological containment laboratories (2019) Specification*:	☐	☐	☐	☐
CA – Canadian Biosafety Handbook, 2nd edition (2016) Specification*:	☐	☐	☐	☐
CA – Canadian Biosafety Guideline: Developing a Comprehensive Biosecurity Plan (2016) Specification*:	☐	☐	☐	☐
US – Biosafety in Microbiological and Biomedical Laboratories, 6th edition (2020) Specification*:	☐	☐	☐	☐
US – Guiding Principles for Biosafety Governance: Ensuring Institutional Compliance with Biosafety, Biocontainment, and Laboratory Biosecurity Regulations and Guidelines (2017) Specification*:	☐	☐	☐	☐
US – A Biosafety Checklist: Developing a culture of biosafety (2015) Specification*:	☐	☐	☐	☐
WHO – Laboratory biosafety manual, 4th edition: Personnel protective equipment (2020) Specification*:	☐	☐	☐	☐

EU – ECDC Technical document on Safe use of personal protective equipment int the treatment of infectious diseases of high consequence (2014) Specification*:	☐	☐	☐	☐
CA – Pathogen Safety Data Sheets (regularly updated) Specification*:	☐	☐	☐	☐
CA – Laboratory Biosafety and Biosecurity portal (updated 2019) Specification*:	☐	☐	☐	☐
WHO – Laboratory biosafety manual, 4th edition: Risk Assessment (2020) Specification*:	☐	☐	☐	☐
International - ISO 22367 Medical laboratories — Application of risk management to medical laboratories (2020) Specification*:	☐	☐	☐	☐
International - ISO 3100 Risk management Guidelines (2018) Specification*:	☐	☐	☐	☐
International – ISO 35001 Biorisk management for laboratories and other related organisations (2019) ** Specification*:	☐	☐	☐	☐
WHO – Laboratory Assessment Tool (2012) Specification*:	☐	☐	☐	☐
EU/EU-project – Integrated European Checklist for Laboratory Biorisk Management in Handling of High Consequence Risk Group 3 and 4 Agents (ECL-Biorisk) (2015) ** Specification*:	☐	☐	☐	☐
SE – Securing Biorisks (Säkra Biorisker) – self-assessment tool (2014) Specification*:	☐	☐	☐	☐
US – National Institutes of Health Biosafety Level 3-Laboratory Certification Requirements (2006) Specification*:	☐	☐	☐	☐
SG – National biosafety standards for maximum containment facilities (2019) Specification*:	☐	☐	☐	☐
WHO – Tuberculosis laboratory biosafety manual (2012) Specification*:	☐	☐	☐	☐
WHO – Laboratory biosafety guidance related to coronavirus disease (COVID-19): Interim guidance (28 January 2021) Specification*:	☐	☐	☐	☐
WHO – Global Action Plan for Poliovirus Containment (GAPIV) (2022) Specification*:	☐	☐	☐	☐

Additional information: