World Health Organization

WHO BioHub System

Biosafety and biosecurity: criteria and operational modalities

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Contents

Introduction

The aim of the World Health Organization (WHO) BioHub System is to implement the timely sharing of biological materials between laboratories and partners globally. This international exchange system will enable rapid assessment of risk and subsequent mitigation measures for epidemic- and pandemic-prone diseases, and thus make global preparedness and response against these diseases more effective.

Laboratories wishing to receive biological materials as part of this international exchange system will need to be accepted by WHO as a Qualified Entity (QE). To acquire QE status, laboratories must meet pre-agreed conditions, including biosafety and biosecurity measures, and various regulations.

Laboratories applying for QE status sign the standard material transfer agreement (SMTA) 2 (non-commercial use) or 3 (all uses including commercial ones), which means that when receiving biological materials with epidemic or pandemic potential (BMEPP) they are deemed to have confirmed proper conformance to the biosafety and biosecurity criteria. This is, in addition to compliance with other relevant WHO guidance documents, and applicable national and international regulations. WHO reserves the right to ask QEs to provide more details for the purpose of application processing and review the QEs' biosafety and biosecurity conformance and performance.

A checklist for QEs is given below, for indication purposes; full details can be found in the document available from the WHO BioHub webpage *(1)*.

Criteria for Qualified Entities

This checklist of criteria can be used to ensure that biosafety and biosecurity measures are in place within your facility, to fulfil the assessment criteria for obtaining QE status:

1. Facility biosafety and biosecurity capacities, capabilities and risk assessments in place and documented.

2. Compliance with "core requirements" as defined in the *WHO Laboratory biosafety manual* 4th edition (LBM4), including observance of good microbiological practice and procedure (GMPP) and standard operating procedures (SOPs).

3. Compliance with "heightened control measures", as defined in the LBM4 and as determined by the risk assessment for the planned experiments.

4. Where applicable, compliance with "maximum containment measures", as defined in the LBM4 and as determined by the risk assessment for the planned experiments.

5. A complete biosafety manual in place, containing institutional policies, programmes and plans as well as responsibilities of biosafety personnel and other staff.

6. A biosecurity plan in place, outlining the security measures, including physical security of the facility, access restrictions, information control and personnel reliability.

7. Commitment and a transparent regime in place to address dual-use research of concern (DURC) and report such research to WHO.

8. Training programme, competency assessments and associated records in place.

9. Medical surveillance programme (occupational health) in place.

10. Emergency and incident response plan in place.

11. Incident reporting system and records in place.

12. Inventory control system and records in place.

13. Records of audits and inspections (internal and external) in place.

14. Maintenance and servicing programme for facility, equipment and technical installations in place.

15. Transportation systems in place, including export and import permits.

The rest of this document provides information on these criteria and related guidance documents.

1. Biosafety, biosecurity and risk assessment

Biosafety and biosecurity are fundamental for protecting the laboratory workforce, the public and the environment from exposure to and inadvertent or intentional release of harmful biological agents. A systematic approach to biosafety and biosecurity programme management that reflects a four-element cycle – planning, assessment, implementation, and review and improvement (Fig. 1) – should be implemented. This approach should be carried out in a manner commensurate with the assessed risk, which would vary substantially, depending on factors such as the characteristics of the biological agent, volume and titre being used, and the procedures being carried out.

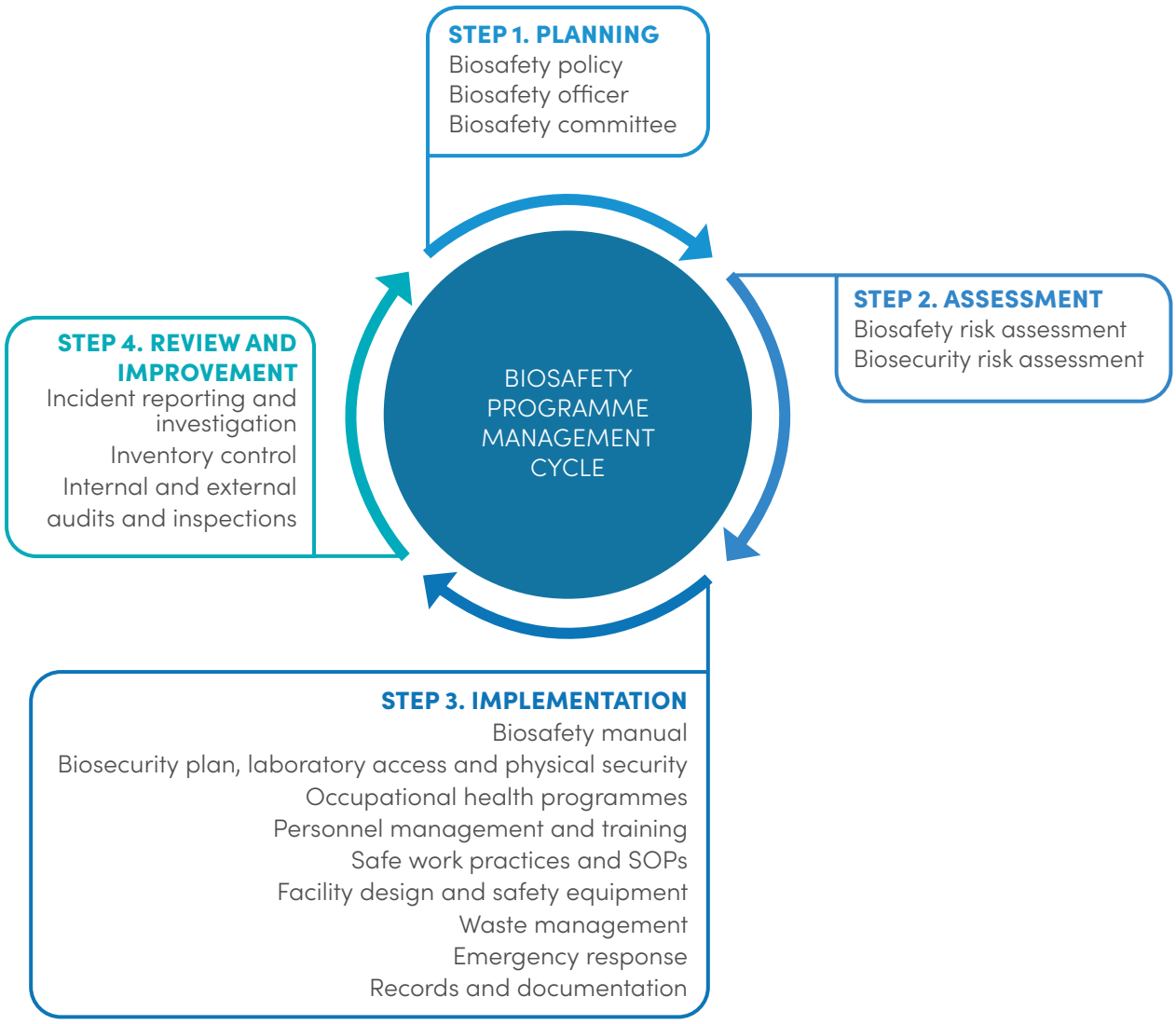

Fig. 1. Biosafety programme management cycle

Comprehensive details of laboratory biosafety relevant to all biological agents are described in the newly published WHO *Laboratory biosafety manual* 4th edition (LBM4) *(2)*. The LBM4 and associated monographs contain useful guidance and templates, including biosafety and biosecurity risk assessments *(3)* and evaluations with potential for dual-use research of concern *(4)*. Also available is specific and concrete guidance for the handling and transport of specified infectious substances such as SARS-CoV-2 virus; for example, WHO's *Laboratory biosafety guidance related to coronavirus disease (COVID-19) (5)*.

Specific guidance on laboratory biosecurity is available *(6)*, but is currently being revised.

The criteria required for QE approval conform with the LBM4 specifications, which build on the risk assessment framework. A thorough, evidence-based and accountable assessment of the risks allows risk control measures to be proportionate to the actual risk of working with biological agents on a case-by-case basis, taking into account factors such as procedures, volume and titre that substantially alter the risk and thus dictate an appropriate risk control strategy. This is in contrast to the conventional direct equation of the risk (hazard) group of the pathogen and biosafety (containment) level.

1.1 Risk assessment

All QEs should be able to demonstrate their capabilities to perform and document a risk assessment for receiving, handling and storing any materials, including proper selection and implementation of risk control measures, based on the proposed research plan. The risk assessment should be regularly reviewed as part of the risk assessment cycle (Fig. 2).

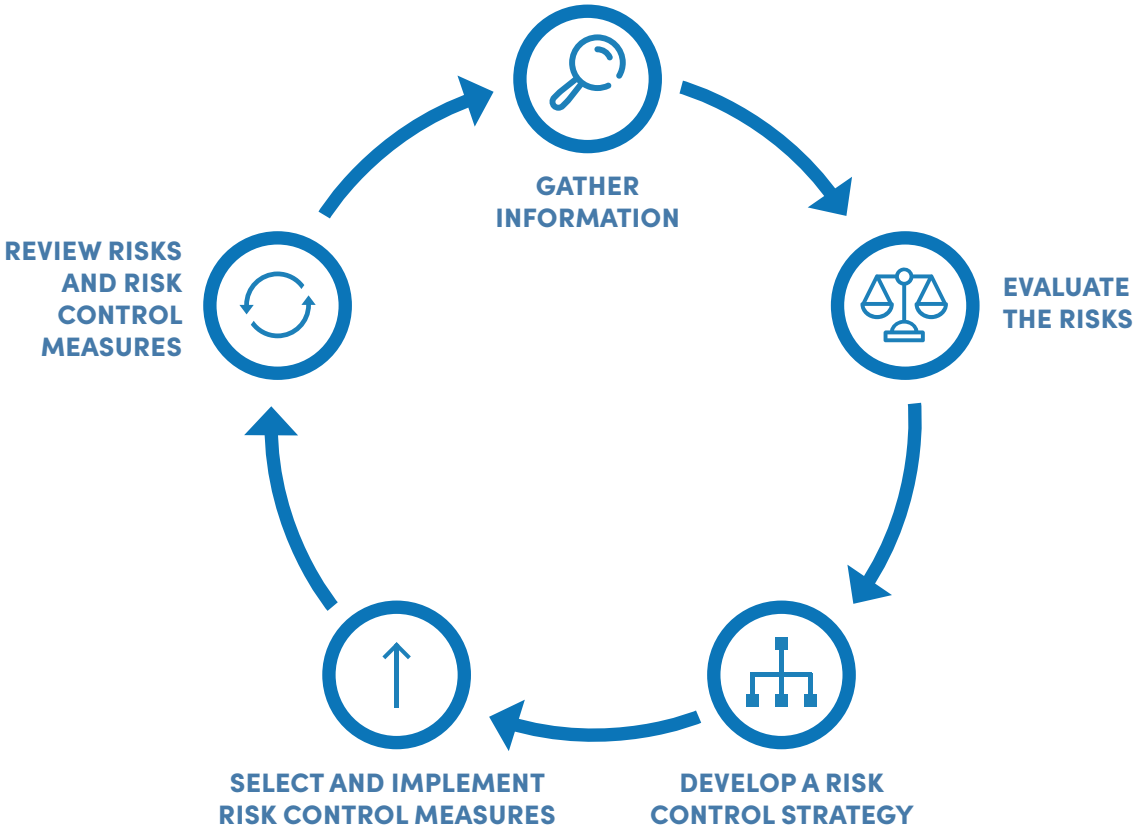

Fig. 2. Risk assessment cycle

A QE should be able to present a brief outline of the planned study and confirm that a risk assessment has been performed and documented, with proper control measures in place. WHO retains the right to request further details in case of safety and security concerns. Annex 1 contains a biosafety risk assessment template, to illustrate the process and facilitate the risk assessment. Detailed templates and useful practical examples are available in the risk assessment monograph of the LBM4 *(3)*.

2. Core requirements

Core requirements are a set of operational and physical items that form the foundation and are an integral part of biosafety in all laboratories. Core requirements for all facilities working with pathogenic biological agents and materials include the following:

- **Good microbiological practice and procedure (GMPP):** a set of SOPs or code of practice that is applicable to all types of activities with biological agents.
- **Personnel competence and training:** including general familiarization and awareness training, job-specific training, and safety and security training, to ensure competent and safety-conscious laboratory personnel.
- **Facility design:** includes features such as ensuring ample space, handwashing facilities, signage, access permission, impermeable surfaces, adequate lighting, first aid supplies, reliable electricity supply and ventilation (a full list of facility design features is given in the LBM4).
- **Specimen receipt and storage:** a set of risk control measures in place for the receipt, storage and inactivation (including verification of inactivation) of specimens.
- **Internal and external transport:** procedures for transferring or transporting infectious substances within or between laboratories in a way that minimizes the potential for drop, spillage, collision or similar events. Transportation outside the laboratory may be subject to various national and international regulations.
- **Decontamination and waste management:** core requirements for the handling of contaminated waste material require processes for the identification, segregation or packing before decontamination, disposal or transportation.
- **Personal protective equipment (PPE):** procedures and application for the correct donning, use, doffing, decontamination and disposal of required wearable equipment or clothing (e.g. laboratory coats, gloves, sensible footwear and eye protection).
- **Laboratory equipment:** all personnel operating or maintaining equipment sufficiently trained and able to demonstrate proficiency; records kept detailing equipment purchase, use, maintenance, validation and calibration procedures and their results.
- **Emergency or incident response:** SOPs in place and to be followed in case of possible emergency scenarios. Personnel must be trained in these procedures and have periodic refresher training in order to maintain competency. First aid kits and equipment must be available and easily accessible. All incidents must be reported, documented and investigated.
- **Occupational health:** the health of laboratory personnel adequately checked and reported to ensure the safety, health and well-being of employees.

A QE should conform with all the core requirements set out in the LBM4.

3. Heightened control measures

In addition to the core requirements, certain control measures are likely to be needed (e.g. biosafety cabinet and respiratory protection), depending on the outcome of the risk assessment. Other elements such as decontamination and waste handling should be augmented where necessary in response to the assessed risks. In cases of propagation or handling of high titre or volume materials, inward directional airflow should be maintained, as guided by the risk assessment. For SARS-CoV-2, specific interim biosafety guidance is available. More details of heightened control measures are set out in Section 4 of the LBM4 and in the associated monograph *Laboratory design and maintenance (7)*.

A QE should be able to demonstrate implementation of heightened control measures based on a thorough assessment of the risks.

4. Maximum containment measures

In exceptional circumstances (e.g. where biological agents with the very highest consequences are being used), maximum containment measures may be required to mitigate risks to personnel and the community. The requirement for maximum containment measures will be determined via a thorough risk assessment. More details on maximum containment measures can be found in Section 5 of the LBM4.

Where applicable, a QE should be able to demonstrate implementation of maximum containment measures based on a thorough assessment of the risks.

5. Biosafety manual

An institutional biosafety policy should be documented. The policy should clearly stipulate the scope, purpose and objectives of the biosafety programme, and the responsibilities of the senior management and key personnel in biosafety. A biosafety policy demonstrates the prominence of and commitment to biosafety and laboratory biosecurity within the organization *(4)*.

A QE should be able to demonstrate a documented biosafety manual for their institution.

6. Biosecurity plan

A biosecurity plan should include the measures to be implemented to prevent the theft, misuse and intentional release of hazardous biological agents. The plan should cover personnel security, information control and physical security of the facility, including access. More detailed information on this can be found in the LBM4 monograph *Biosafety programme management (4)*.

A QE should be able to demonstrate a documented biosecurity plan for their institution.

6.1 Personnel management

The effectiveness of any procedural controls for biosecurity are ultimately determined by the training, capability, reliability and integrity of the personnel. A personnel management programme should be established and implemented, and should include an access approval process and laboratory biosecurity training for all personnel, commensurate with the outcomes of the risk assessment. Security-related roles and responsibilities of personnel in everyday and emergency scenarios should also be defined.

Records of training and competence assessment form part of the documentation required to show how a QE's personnel management system is operating and whether it is operating at a satisfactory level.

6.2 Information control

Proper care should be taken and adequate measures maintained to protect the confidentiality and integrity of sensitive information held in the laboratory that could be used with malevolent intent.

A QE should be able to show how each process is designed and controlled, including what checks are carried out to keep the processes under control.

6.3 Physical security control

Proper physical security countermeasures (proportionate to the assessed risk) should be used to prevent unauthorized access by outside adversaries and to minimize the threat from insiders who do not require access to a particular asset.

A QE should be held accountable for proper implementation of physical security countermeasures that should be well documented and demonstrable.

7. Dual-use research of concern

A QE should be able to demonstrate capacities and an effective regime in assessing the risks posed by inadvertent exposure and release as well as misuse and misapplication (i.e. DURC) inherent to gain-of-function and other genetic modifications. The QE should select appropriate risk control measures to minimize those risks in order to conduct necessary and beneficial life sciences research (e.g. a biosecurity code of conduct).

Annex 2 illustrates a procedural flow of the process, and Annex 3 will help in flagging research of concern. Where planned research is deemed to have DURC potential, the QE in question should report this to WHO before undertaking any research. Consultation with the WHO BioHub System BMEPP Allocation Advisory Group, which is charged with assessing the appropriateness and acceptance of such research, will be required.

8. Training and competency

Training and competency are fundamental to working safely within the laboratory and promoting a safety-conscious culture within a scientific organization. A good training programme will include current and future training needs including biosafety, biosecurity and risk assessment.

A QE should have documentation to show how competency is assessed and the types of training, including refresher training, required and completed by personnel.

9. Medical surveillance programme (occupational health)

A medical surveillance or occupational health programme is required to monitor and document any occurrence or potential occurrence of laboratory exposure to biological agents or release of such agents. This allows preventive measures such as vaccination and post-exposure prophylaxis where possible and practical. It also allows the re-assessment of risks, practices and procedures where a laboratory-associated infection has occurred, and will thus reduce the likelihood of future exposure or release events.

A QE should be able to demonstrate documented evidence that its employing authority takes responsibility for ensuring that the health of laboratory personnel is adequately checked and reported.

10. Emergency and incident response plan

An emergency and incident response plan enables appropriate actions to be taken by individuals within an organization in the event of an emergency such as spillages, power failures and fire. This minimizes the impact of any incident on the health, safety and well-being of individuals, the wider community and environment. An emergency response plan should include responsibilities of individuals, appropriate training and practice drills, and documented procedures.

A QE should have a documented emergency response plan in place.

11. Incident reporting system

An incident response protocol should be documented and followed to ensure proper reporting, and to facilitate investigation, root-cause analysis, corrective action and process improvement.

A QE should document the incident protocol, and keep the report and record of subsequent actions accurate and current.

12. Inventory control system

A QE should be held accountable for the materials received, propagated and manipulated, maintaining a chain-of-custody to track samples from accessioning to disposal.

A QE should keep an accurate and current inventory of biological materials, and be able to present the inventory to WHO upon request.

13. Audits and inspections

13.1 Records of auditing

A system for regular internal audits should be in place to actively identify hazards, deficiencies or areas for improvements. Such a system will help to prevent incidents and accidents. The results of the audits should be directly incorporated into the regular review cycle of the risk assessment.

A QE's management regime should be able to maintain and provide a robust audit trail upon request.

14. Maintenance and servicing

Safe use, maintenance and servicing of equipment reduce the likelihood of accidents or the release of biological agents.

A QE should have SOPs for equipment use, and records of any maintenance, servicing, validation and calibration procedures carried out.

15. Transportation systems

For exportation and importation, a QE must meet all the regulatory requirements from the WHO BioHub facility country for exporting the requested item or items (i.e. export permit) and of the destination country (i.e. import permit), whenever such requirements are applicable.

A QE should facilitate the process of transportation, including making the proper arrangements for an import permit where necessary.

References

1. WHO BioHub [website]. Geneva: World Health Organization; 2021 (https://www.who.int/initiatives/who-biohub/).

2. World Health Organization. (2020). Laboratory biosafety manual, 4th ed. World Health Organization. https://apps.who.int/iris/handle/10665/337956. License: CC BY-NC-SA 3.0 IGO

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6. World Health Organization. (2006). Biorisk management : laboratory biosecurity guidance. World Health Organization. https://apps.who.int/iris/handle/10665/69390

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Annex 1 Biosafety risk assessment template

The template shown here is for indicative purposes only. More detailed risk assessment templates are available in the risk assessment section of the World Health Organization *Laboratory biosafety manual*, 4th edition (*1*).

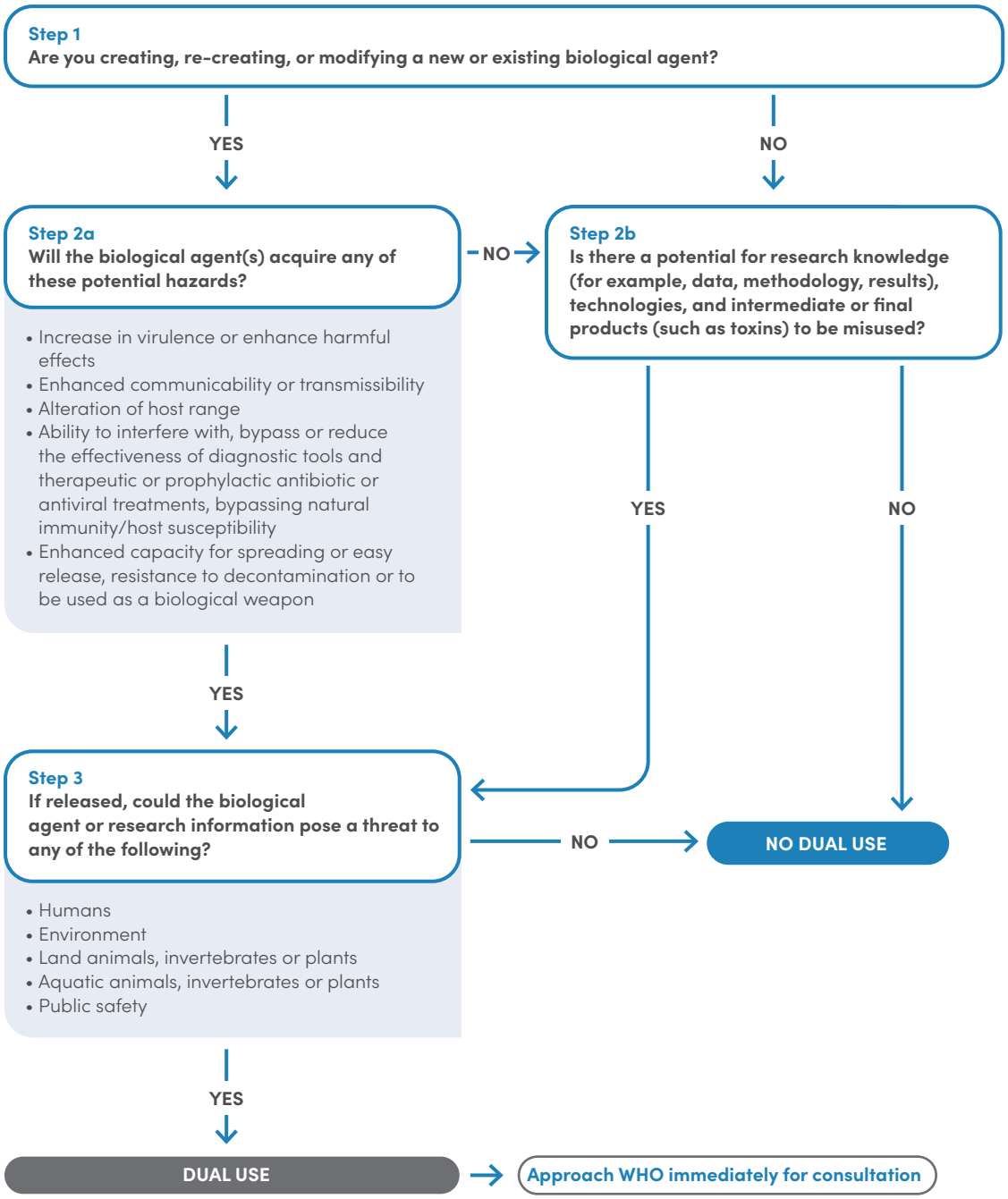
Annex 2 Biosecurity risk assessment template

This template is taken from the World Health Organization *Laboratory biosafety manual*, 4th edition (*1*).

		DESCRIPTION	EXAMPLES
Step 1 – Asset	**Asset inventory**	Inventory of all tangible and intangible assets.	• information or organisms with dual-use potential • animals • floor plans • equipment • software • documented information • personnel • contractors
Step 2 – Risk identification	**Risk scenario**	Description of what could happen as a result of an incident occurring with the asset as listed below.	• deliberate or accidental loss • unauthorized release • diversion • sabotage • theft • espionage • misuse • terrorism • extortion
	Likelihood	General indication of the possibility of the risk if a risk control measure is not in place. Consider including: • potential adversary (e.g. internal personnel, external individuals) • their motivation and capability to act • predicted or known frequency of the scenario	• very low • low • moderate • high • very high
	Consequences	Indication of the consequences to relevant populations and the extent of the effects.	• harm, disease or death of animals • harm, disease or death of humans • financial losses • negative effect on the reputation of the organization
Step 3 – Risk control	**Risk control measures**	Description of the applicable risk control strategies to be implemented. Consideration should be given to prevention and response actions.	Personnel suitability: • security screening • insider threat training Access controls: • security barriers • access control systems • entry and exit records Emergency response: • release recovery procedure incident
	Vulnerability assessment	Assessment of the effectiveness of the risk control strategy on the identified weaknesses in relation to the impact of the likelihood and consequences.	• very low • low • moderate • high • very high
Step 4 – Risk acceptance and review	**Strategy review**	Based on the risk assessment and risk control measure, determine the overall risk associated with the asset. Review whether the risk is acceptable. Where the risk is unacceptable, a cost–benefit analysis may help determine if additional risk control measures are necessary. The biosecurity risk assessment should be routinely reviewed and updated when changes affect the risk.	• acceptable • not acceptable

Annex 3 Decision tree to evaluate dual-use potential

This decision tree is taken from the biosafety programme management section of the World Health Organization *Laboratory biosafety manual*, 4th edition (*1*).



Annex 4 Qualified entity requirements checklist

This checklist is for qualified entities wishing to receive biological materials with epidemic or pandemic potential.

Checklist for QEs wishing to receive BMEPP

- ☐ **Biosafety and biosecurity risk assessment(s) are completed for the work to be carried out with the BMEPP to be received**
- ☐ **Facility for storing and working with the BMEPP meets core requirements as outlined in the *Laboratory biosafety manual* 4th edition (LBM4)**
- ☐ **Facility for working with the BMEPP meets heightened control measures as outlined in the LBM4, where required**
- ☐ **Facility for working with the BMEPP meets maximum containment measures as outlined in the LBM4, where required**
- ☐ **Biosafety manual, containing institutional policies, programmes and plans as well as responsibilities of biosafety personnel, is in place**
- ☐ **Biosecurity plan, outlining the security measures including personnel reliability, is in place**
- ☐ **Commitment and a transparent regime are in place to address dual-use research of concern (DURC)**
- ☐ **Training programme, competency assessments and records are in place**
- ☐ **Medical surveillance programme(s) is in place**
- ☐ **Emergency response plan is in place**
- ☐ **Incident reporting system and records are in place**
- ☐ **Inventory system is in place**
- ☐ **Have records of audits and inspections**
- ☐ **Have a maintenance and servicing programme for equipment and technical installations**
- ☐ **Have export and import permits**

Reference for annexes

1. World Health Organization. (2020). Laboratory biosafety manual, 4th ed. World Health Organization. https://apps.who.int/iris/handle/10665/337956. License: CC BY-NC-SA 3.0 IGO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