MINISTRY OF HEALTH OF THE REPUBLIC OF KAZAKHSTAN

NATIONAL SCIENTIFIC CENTRE FOR ESPECIALLY DANGEROUS INFECTIONS
NAMED AFTER MASGUT AIKIMBAYEV

TRAINING MANUAL

APPLIED LABORATORY BIOSAFETY

Edited by Dr. T. K. Yerubayev

Almaty – 2023

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Annotation
This training manual was developed by the Department of Biosafety and Biosecurity at the National Scientific Centre for Especially Dangerous Infections named after M. Aikimbayev as a training material for laboratory specialists, lecturers and trainers, who train personnel in laboratory biosafety and biosecurity. The manual can be used for self-training by biomedical specialists, heads of laboratories, managers of health care organizations with laboratory units.
The aim of this manual is to provide theoretical training on policies on handling pathogenic biological agents and contaminated material, biocontainment, biological risk management, individual protection of personnel and to provide practical approaches to prevent and/or reduce biological threats in the laboratory.
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ABBREVIATIONS

AMP model	Assessment, Mitigation, Performance
AR	Agglutination Reaction
BSL-2 / BSL-3	Biosafety Level –2 / Biosafety Level – 3
CSCD	Container for the Safe Collection and Disposal of medical waste
DNA	Deoxyribonucleic acid
ELISA	Enzyme-Linked Immunosorbent Assay
EU	European Union
GLP	Good Laboratory Practice
GMO / GMM	Genetically modified organism / microorganism
GMPP	Good Microbiological Practices and Procedures
HEPA	High-efficiency particulate air
HVAC	Heating, ventilation and air conditioning system
ID	Infectious dose
ISO	International Organization for Standardization
MoH RK	Ministry of Health of the Republic of Kazakhstan
MW	Medical Waste
NSCEDI	National Scientific Centre for Especially Dangerous Infections
OHSAS	Occupational health and safety Assessment Series
PAPR	Powered air-purifying respirator
PBA	Pathogenic biological agent
PCR	Polymerase chain reaction
PDI	Particularly dangerous infection
PPE	Personal protective equipment
PSDS	Pathogen Safety Data Sheet
QMS	Quality management system
SHW	Solid Household Waste
SOP	Standard operating procedure
UV	Ultraviolet
WHO	World Health Organization

TERMS AND DEFINITIONS

Acceptable risk – The minimum amount of risk that is acceptable for each specific situation, taking into account the expected benefits of the planned activities.

Aerosol – A suspension of liquid or solid particles in air or gas.

Airborne infections – Any infectious disease, characteristic features of which are: aspirational transmission of the causative agent and its primary location on mucous membranes of respiratory tracts.

Audit (OHSAS 18001:2007) – A systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled..

Autoclave – Device usable to sterilise medical instruments, materials or wastes with use of hot water vapour, at temperature of 121o C or higher, under pressure.

Biocontainment – A set of measures intended to preclude or minimise release of any infectious pathogens into the environment or into any other laboratory facilities not intended for this originally.

Biohazard – Potential source of any harm caused by biological agents or toxins on personnel, animals, and the environment.

Biological agent / disease-causing agent – Any microorganism, including those that have been genetically modified, cell cultures and endoparasites, which may be able to provoke any infection, allergy or toxicity in humans, animals or plants.

Biological risk – Combination of the probability of occurrence of harm and the severity of that harm, where the source of harm is a biological agent or toxin.

Biological risk assessment – The process of evaluating the risk(s) arising from a biohazard(s), taking into account the adequacy of any existing controls, and deciding whether or not the risk(s) is acceptable.

Biological safety cabinet – Specially designed cabinet/box, a protective device to protect the operator and the environment from biological hazards through the use of directional air flow and air filters. Serves to create a dust-free/microbial-free air environment with laminar airflow for safe handling of cell cultures and pathogens.

Biorisk management – An organisation's management system that ensures the development and implementation of the organisation's biosafety policy, including the identification of biorisk and the identification of effective risk control measures to reduce risk to an acceptable level.

Biosafety – Biological safety combines together development of theoretical principles and practice of protection of humans, animals and the environment from hazardous biological agents during its handling and study.

Biosafety cabinet class I – The Class I biosafety cabinet/box with open air inlet and low negative pressure, equipped with ventilation systems and HEPA filters for cleaning the exhaust air. The Class

I biosafety cabinet will provide personnel and environmental protection, but not product protection.

Biosafety cabinet class II – The Class II biological cabinet is an open-front, ventilated cabinet. This cabinet provides a HEPA filtered, recirculated mass airflow within the work space. The exhaust air from the cabinet is also filtered by HEPA filters. Thus, the Class II biosafety cabinet will provide personnel, environment and product protection. While HEPA filters are effective for trapping particulates and infectious agents, these filters will not capture volatile chemicals or gases.

Biosafety culture – An informal set of values, beliefs and behaviours instilled and encouraged in an open and trusting atmosphere by organisations to support or improve best practice in laboratory biosafety.

Biosafety officer – Responsible person for effective implementation of biosecurity (and possibly biosafety) programmes in the laboratory.

Biosecurity – Laboratory biosecurity describes the protection, control and accountability for biological agents and toxins within laboratories, in order to prevent their loss, theft, misuse, diversion of, unauthorised access or any intended unauthorised release.

Chemical sterilization – Process of sterilization using gases or liquid chemicals (disinfectants).

Contamination – Contamination is the presence of an unwanted constituent in another material, metal, chemical or mixture, often at the trace level.

Corrective measures (OHSAS 18001:2007) – Actions aimed at eliminating the cause of the identified nonconformity or other undesirable situation.

Decontamination, syn. disinfection (ISO 15190:2003) – Procedure that eliminates or reduces biological agents and toxins to a safe level with respect to the transmission of infection or other adverse effects.

Disinfectants – Chemical agents capable of destroying or inhibiting pathogenic biological agents on surfaces or in liquid.

Genetically modified microorganisms (GMM) EC Directive 98/81/EC) – A microorganism whose genetic material has been altered by mechanisms not found in nature through natural crossing and/ or recombination.

Good Laboratory Practice (GLP) – Good Laboratory Practice (GLP) is a quality system concerned with the organisational process and the conditions under which laboratory work is planned, performed, monitored, recorded, archived and reported.

Good Microbiological Practices and Procedures – Basic laboratory practices used to avoid or minimise exposure to biological agents, including general rules of conduct and aseptic practices that should always be observed in the laboratory.

Heat sterilization – Process of sterilisation using heat.

HEPA filter (High efficiency particulate air filter) – Any filter manufactured with use of the appropriate technology and of appropriate materials for protection from airborne particles; with a filtration efficacy rate of not less than 99.97%.

HVAC system – Heating, ventilation and air conditioning system used to handle and condition air in a building..

Incident – Unintended event during laboratory work with pathogens giving rise to harm on human or environment, animals and plants.

Infection – Penetration into and development or proliferation of any infective agent in any living organism.

Infectious dose (ID) – The amount of a biological agent required to cause an infection in a host is measured in microbial cells/ml. Defined as the ID50, the dose that will cause infection in 50% of those exposed.

Laboratory-acquired infections – Infections acquired within the laboratory.

Laboratory procedures leading to the generation of aerosols – Any procedure that intentionally or unintentionally leads to the formation of liquid or solid particles that become suspended in the air (aerosols).

Laminar airflow – Unidirectional airflow through the work area often referred to as turbulence-free airflow; steady, unidirectional micro-turbulence flow; or mass airflow.

Nonconformity (OHSAS 18001:2007) – When a process does not meet the requirements.

Observation – A medical monitoring of the health of individuals who are within a quarantine zone, but are intending to quit it after the monitoring period is over.

Particularly dangerous infections (PDI) – Infectious diseases with exceptional epidemic danger, suddenly appear and spread among a large mass of the population in the shortest possible time, proceed with a severe clinic and are characterised by high mortality.

Pathogen / pathogenic micro-organism; agent of disease – A microorganism (including bacteria, viruses, rickettsiae, parasites, fungi) or other agent, such as a proteinaceous infectious particle (prion) that can cause disease in humans, animals or plants.

Pathogenicity groups – According to the WHO pathogenicity groups are classification of infective microorganisms based on their relative hazard. Under national pathogen classification, top hazard-level biological agents are classified as Pathogenicity Group I, while those which are virtually hazard-free are classified as Pathogenicity Group IV. It should be mentioned that appropriate classification applicable by WHO and overwhelming majority of other countries is quite the reverse to the above: the top-hazard pathogens are classified as Group 4, and those virtually non-hazardous are treated as Group 1.

Personal Protective Clothing and Equipment (PPE) (ISO 15190:2003) – PPE is specialized clothing or equipment worn by a worker for protection against a hazard. Material, including clothing (e.g. gown, gloves, respirators, safety glasses), used to prevent exposure to or contamination of a person by chemical or biological matter.

Personal reliability – An assurance that individuals with access to dangerous pathogens are trustworthy, reliable and physically and mentally competent.

Respirator – A respirator is a device designed to protect the wearer from inhaling harmful dusts, fumes, vapours, gases and microorganisms.

Risk – Combination of the probability of occurrence of harm and the severity of that harm.

Risk groups – According to the World Health Organization (WHO) risk groups are classification of infective microorganisms based on their relative hazard.

Standard Operating Procedure (SOP) – A set of written instructions that document a routine or repetitive activity followed by an organisation.

Steam sterilisation – Process of sterilisation using steam (e.g., autoclave).

Sterilization – Sterilisation refers to any process that effectively kills or eliminates biological agents (such as fungi, bacteria, viruses, spore forms, etc.).

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

Transmission of infection – The way the causative agent of an infectious or parasitic disease moves from a contaminated organism into a susceptible one.

Vaccination –Putting of an antigenic substance into the body in order to provide immunity against a disease; such substance is intended to prevent or mitigate the effects of any given infection.

FOREWORD

The issue of biosafety, linked to the protection of the environment and human health and the maintenance of physical and social activity, affects the interests of every citizen and, more generally, the whole state. It is a basic principle that no research project can be deemed so important as to compromise the safety of humans, animals, plants or the environment when dealing with pathogens and pathogen-contaminated biological material [1]. This principle also applies to the routine activities of diagnostic-, industrial-, educational- and other laboratories. It should be understood that even alone the simple storing of pathogens within a laboratory creates the risk of their intentional or unintentional release into the environment, internal laboratory contamination of personnel, contamination of facilities and equipment and, consequently, contamination of humans and animals. If a pathogen can be transmitted from person to person or from animal to animal, there is a risk of mass spread of infection, with social, political and economic consequences.

Laboratory biosafety and biosecurity requirements aim at the prevention or reduction of biological hazards and aim to provide a safe laboratory environment for personnel. The establishment of an effective biological risk management system is an essential link in the functioning of the laboratory and an integral part of the organizational structure of the laboratory [2, 3].

The training modules of this manual demonstrate the requirements set by national regulatory structures and international organisations for biosafety and provide practical methods to implement a biological risk management system in the laboratory..

PART I. INTRODUCTION

Biological safety is the state of protection of people and individual components of the natural environment (atmospheric air, surface and ground waters, land surface and soil layer, flora and fauna and other organisms (hereinafter collectively termed individual components of the natural environment)) from biological hazards, including those ensured by biological protection measures [4-6].

Biosafety regulations in the laboratory are intended to protect laboratory personnel and the public from unintentional and intentional exposure to pathogenic biological agents. All necessary biosafety and biosecurity measures in the laboratory are implemented within the framework of the biorisk management system and through the development of a safety culture.

The legal basis for the biorisk management system is the existing laws and other normative legal acts in the field of biosafety, as well as international treaties and agreements to which the Republic of Kazakhstan is a party [2, 4, 7, 8, 9, 10, 11]:

- Code of the Republic of Kazakhstan on Public Health and the Health Care System, 2020.
- Law on Biosecurity of the Republic of Kazakhstan, 2022.
- Sanitary Rules «Sanitary and Epidemiological Requirements for Laboratories Using Potentially Hazardous Chemicals and Biological Substances», MoH Order No. 105 of 15.10.2021.
- Sanitary Rules «Sanitary and Epidemiological Requirements for Healthcare Facilities» by Order No. 96 of the Ministry of Health of RK dated 11.08.2020.
- Sanitary Rules «Sanitary and Epidemiological Requirements for Collection, Use, Utilisation, Decontamination, Transportation, Storage and Disposal of Production and Consumption Waste»

Order No. 331 of the MH RK dated 25.12.2020.

- World Health Organization. Laboratory biosafety manual. Fourth edition. Geneva: World Health Organization; 2020.
- ISO 35001 «Biorisk management for laboratories and other related organisations», 2019.

The aim of biosafety is to eliminate or progressively reduce to the minimum acceptable level of the risk of exposure of personnel and the installing of infrastructure by the organisation to contain biological hazards.

The objective is achieved by 1) a risk-based approach to biological hazards in biorisk management, 2) identifying and implementing effective measures to prevent or reduce biological risks, and 3) increasing the competence of laboratory personnel through systematic and effective training in all biosafety issues.

The priorities for biosecurity are [2, 3, 49]:

- establishing a biorisk management system;
- training and professional development of staff;
- prevention of emergencies involving biological agents through monitoring and forecasting in the area of biosafety.

In a laboratory that handles pathogenic microorganisms and hazardous infectious material it must be ensured that an effective biorisk management system is installed. This includes several steps such as the commitment and interest of senior management in biosafety and biosecurity and a focus on continuous improvement. Management shall ensure the development and approval of a laboratory biorisk management policy that clearly articulates the overall objectives of biorisk management and the focus on protecting personnel, the public, and the environment from biological agents and toxins that are actively used or stored in the facility. The policy should be commensurate with the nature and extent of the institution's biological risk factors and activities [3, 12].

The commitment of the organisation's management is expressed by providing appropriate administrative, financial, logistical, and human

resources; prioritising and communicating biosafety and biosecurity policies; ensuring that continuous improvement is the task of every staff member in the organisation; conducting periodic biorisk assessment and monitoring staff compliance with biosafety responsibilities; and providing training and education courses on safe laboratory work to staff.

The organization's biosafety and biosecurity activities, including the mechanism and methods for implementing the biorisk management system, shall be planned and described in the Laboratory Biosafety Manual [2, 3, 13, 14].

PART II.
BIOLOGICAL RISK MANAGEMENT

The biological risk management system is governed by international and national requirements and standards, is proactive in nature and aims at reducing the risk of exposure to biological hazards when working with pathogenic biological agents (hereinafter PBA) to an acceptable or tolerable level [3, 12].

As recommended in the WHO Laboratory Biosafety Manual [2] the biological risk management system is implemented in five stages:

1. Information gathering and identification of biological risks.
2. Biorisk assessment.
3. Development of risk control measures.
4. Implementation of control measures in the laboratory to reduce biorisk.
5. Assessment of the effectiveness of control measures.

National requirements for biorisk management are also based on a biological risk assessment procedure for sensitive laboratory procedures and include a biorisk assessment based on the likelihood and severity of exposure to a biological agent, implementation of improvement measures and monitoring the effectiveness of biorisk mitigation measures [4].

Our recommended biorisk management framework (Figure 1) is the AMP model (Assessment, Mitigation, Performance), which has a risk-based approach and consists of three components [12, 15, 16]:

- biological risk assessment;
- biorisk control or biorisk mitigation measures;
- assessment of the effectiveness of control measures.

No biorisk management system is complete without including these three components.

The first step in the biorisk assessment involves collecting and analysing information on the biological pathogen and/or material, assessing the probability of exposure to the pathogen against the available control measures and finally determining the level of the biological risk. The biological risk assessment procedure is documented in the form of a Biological Risk Assessment Report with a conclusion that the biorisk is acceptable or unacceptable (a template of this document is presented in Appendix 1). The Biological Risk Assessment Report shall describe all procedural steps of the study with a biorisk assessment for each procedure. In case of a biorisk assessment of special or difficult work with pathogenic material additional experts shall be involved and the Biological Risk Assessment Report shall be approved by the laboratory leaders or the local Biosafety and Biosecurity Committee.

In the second step, the results of the biorisk assessment shall be used to develop measures to reduce the identified biorisks to an acceptable (tolerable) level that provides conditions to protect personnel and the laboratory environment from exposure to biological hazards. All recommended biorisk mitigation measures, both existing and additional, shall be indicated in the Biorisk Assessment Report (Annex 1).

The third step is to analyse the effectiveness of biorisk mitigation measures in the form of internal and external evaluations. Internal assessments of biological risks are carried out by laboratories handling pathogenic biological agents to assess the quality of their own performance [5]. External assessments of biological risks are carried out by government agencies within the scope of their competence.

Quantitative indicator-based biorisk assessment requires the development of digital programmes that take into account all the factors available in the laboratory and influence the probability of



Figure 1 – Biorisk management system

exposure to biorisk. The introduction of digital biorisk assessment programmes is a matter of the near future.

The biological risk assessment procedure is carried out in the laboratory on a continuous basis at all stages of a lifecycle of a laboratory:

1) when a new laboratory is commissioned, new laboratory rooms are opened, laboratory rooms are redesigned or their functional purpose is changed;

2) in an existing operative laboratory before the handling of pathogenic biological agents for which a risk assessment has not been carried out yet;

3) when starting a new project that involves the handling of pathogenic biological agents;

4) when introducing new types of work and methods in the laboratory for which no risk assessment has been carried out;

5) when starting the work with a new pathogenic biological agent;

6) when, there is a significant change in current procedures related to the handling of pathogenic biological agents.

The persons responsible for carrying out the biological risk assessment are [2, 3, 11, 14]:

1) the laboratory manager and/or project manager of a project involving the handling of pathogenic biological agents;

2) a plant biosafety specialist in conjunction with the laboratory manager and/or project manager of a project involving the handling of pathogenic biological agents;

3) biosafety experts with expertise in the issues raised in the test protocol or a local biosafety/biosecurity committee shall be involved if the planned laboratory procedure is of high risk.

Laboratory managers and laboratory specialists participate in or conduct biological risk assessments in accordance with current procedures and support the biosafety officer in conducting the biorisk assessment.

In addition to assessing biorisk, the laboratory should conduct annual internal audits to monitor biosafety and biosecurity compliance and assess staff competencies [4]. This handbook will present an algorithm for conducting a biorisk assessment of laboratory procedures and how to perform an internal biosafety and biosecurity audit of the laboratory.

An essential tool and manual for each individual laboratory is the Laboratory Biosafety and Biosecurity Manual, which describes the essential elements of a biosafety and biosecurity programme and a biological risk management methodology.

The Biosafety Manual shall include the following sections:

- responsibilities of management and staff for biosafety compliance and control and allocation of responsibilities;
- characterisation of biological pathogens and biological materials handled by the laboratory;
- biorisk assessment methodology, description of laboratory procedures;
- description and monitoring of biorisk mitigation measures;
- conducting an internal biosafety and biosecurity audit;
- disinfection regime of the laboratory (premises, waste, protective clothing and PPE, equipment and engineering systems);
- medical waste management scheme;
- transport and reception of biological material;
- emergency and non-emergency response procedures;
- medical supervision of staff.

When new methods and techniques are developed or introduced in the laboratory that require enhanced biosafety and/or biosecurity measures, the Biosafety Manual shall be amended accordingly.

2.1 Biological hazards/threats: concept, identification

Biorisk assessment is based on an assessment of the likelihood of a harmful event occurring and the extent of the consequences of a harmful event when the source of that event is a biological agent or toxin.

A fundamental factor in conducting a biorisk assessment is to determine

what harms and consequences a biorisk may cause. To understand this one exactly needs to know what the specification of the biological agent or biological material used in a laboratory procedure are.

In the conventional sense, **harm** is some adverse consequence of exposure to an object of value. In biosecurity terms, harm is an adverse effect on human health, animals, plants, the environment and/or property caused by a pathogenic microorganism.

The source of harm may be the pathogenicity factors of the biological agent itself, but also unintentional or malicious exposure to laboratory equipment, misuse of laboratory techniques, accidental spillage or other diversion of hazardous biological material, loss, theft, contamination by unauthorized persons through unauthorized access to the laboratory, etc. count as sources of harm.

A situation that could potentially cause harm is called a hazard.

Remember: There is no danger without harm!

The potential source of harmful effects caused by biological materials is called **a biohazard**.

Obviously, the mere presence of a pathogen or other hazardous biological materials in a laboratory poses a biological hazard. When any work is carried out on the pathogen, the hazard level increases. However, not every biological material is hazardous. A distinction is made between biological material and hazardous biological material.

Biological material is material that contains genetic information and is capable of reproduction. For example, wheat grains are certainly biological material. They contain wheat DNA and, when planted, are capable of germinating and producing ears with new grains, i.e. they are capable of reproduction. However, wheat grains pose no biological hazard: they are used in the nutrition of both humans and animals. However, if infected with ergot (Secale cornutum, a parasitic fungus), wheat grains can cause ergotism - food poisoning by ergot alkaloids - in humans and animals.

Thus, **hazardous biological material** is material containing **biological agents** (pathogens) or their adverse health effects ***(toxins and***

allergens).

Quite often the term pathogen and biological agent are used synonymously, including in the definition above. In fact, there is a difference in the terms.

The term **pathogen** is a rather old one, having been used in biology since the 1880s. The term was used to describe any organism capable of causing disease. Nowadays, the term pathogen refers to a micro-organism that has the property of being infectious. **Pathogens** include bacteria, viruses, protozoa, prions, viroids and fungi.

What are biological agents? Pathogenic biological agents (PBAs) are micro-organisms (bacteria, viruses, viroids, rickettsiae, chlamydiae, protozoa, fungi, mycoplasmas, phytoplasmas, endo- and ectoparasites), poisons of biological and plant origin (toxins), helminthes, or nematodes that can cause an infective or parasitological pathological process in human, animal or plant organisms.

Remember: A pure culture of microorganisms (e.g. an agar culture of Yersinia pestis) is both a hazardous biological material and a pathogenic biological agent.

All pathogenic (hazardous) biological agents can be divided into 9 groups according to their biological nature (Table 1).

Table 1 – Groups of dangerous biological agents

Group name	Group description
Bacteria	Single-celled organisms that lack a formalised cell nucleus and membrane organoids such as the endoplasmic reticulum and mitochondria and which exist in three phenotypes based on the structure of the cell wall: Gram-negative bacilli and cocci, Gram-positive bacilli and cocci and Mycoplasmas (no cell wall). Bacteria that cause infectious diseases in humans, animals and plants are referred to as pathogens. Some pathogens are capable of causing disease in humans and animals (zoonoses) or in humans and plants (phytonoses).

Viruses	A virus is a tiny (submicroscopic) pathogen that has no metabolism of its own and is unable to reproduce outside the host cell. Viruses infect animals, including humans, plants and bacteria. Viruses that parasitise in bacterial cells are called bacteriophages. Some viruses have been found that can replicate only in the presence of other viruses (satellite viruses), such as the hepatitis D virus, which multiplies only in cells already infected with hepatitis B virus. Viruses are classified according to the type of nucleic acids contained in the virion and their multiplication strategy: DNA viruses (single stranded and double stranded), RNA viruses (single stranded positive chain, single stranded reverse transcribed and double stranded) and sub-viral agents.
Fungi	A Fungi is a eukaryote with its typical organelles, including the nucleus, vacuoles and mitochondria, and are possessing both, properties characteristic of animals (presence of chitin in the shell, sterols in the cytoplasmic membrane and glycogen in the cytoplasm) and plants (presence of a cell wall composed of polysaccharides, reproduction by spores, immobility in the vegetative state). Pathogenic fungi belong to the divisions Zygomycetes (mucor or white mould), Deuteromycetes (penicillium or mould) or Ascomycetes (yeast).
Parasites (protozoa and helminths)	Protozoa or helminths that live on or inside a larger host organism.
Toxins	A poison of biological origin that causes pathological conditions in the human body.
Recombinant DNA	Genetically engineered DNA obtained by transferring or splicing genetic material from one species into the genome of a host organism of another species. Such DNA becomes part of the genome of the host and begins to reproduce itself.

Cell lines	Populations of cells from a multicellular organism that, due to a mutation, can continue to undergo constant division.
Human and animal bodily fluids and tissues	Human/animal organs and tissues, blood and blood components, samples of human/animal biological materials. Samples of human biological materials - samples of human cells, tissues, biological fluids, secretions, products of human vital functions, physiological and pathological secretions, smears, scrapes, wipes used for diagnostic, scientific purposes, research. Human bodily fluids are fluids produced by the human body (pus, blood, lymph, sputum, bile, colostrum, urine, prostate secretion, mucus membranes, synovial fluid, sperm, cerebrospinal fluid, tissue fluid, pleural fluid, nasal mucus, sweat, transudate, ear wax and exudate).

Identifying the hazards associated with the storage or handling of biological material is t***he first step*** in the biological risk assessment procedure.

The main sources of biohazards in laboratories include:

- pathogens of pathogenicity groups 1-2, including viruses and bacteria - agents of especially dangerous infections (EDIs), emerging and re-emerging infections;
- pathogenic biological agents resistant to modern antibacterial agents and disinfectants;
- genetically modified organisms (GMOs) including industrial micro-organisms, recombinant strains, cell cultures and genetic constructs;
- the attackers are products of microorganisms - toxins, enzymes, prions, bioregulators of protein nature (cytokines), superantigens, enzymes, antibodies, etc;
- class B and C medical waste - potentially hazardous

substances which, due to their physical, chemical, biological or toxicological properties, pose a risk to humans, farm animals or plant life or health.

The national legislation of the Republic of Kazakhstan differentiates micro-organisms in terms of hazard and severity of consequences for human health into pathogenicity groups [4]:

1) **1. Pathogenicity Group I** - pathogenic biological agents that cause particularly dangerous infectious diseases in humans and/or animals with a high mortality rate, easily spread from infected to healthy organisms, for which vaccines and effective therapies are usually not available;

2. **Pathogenicity Group II** - pathogenic biological agents that cause infectious and/or parasitic diseases in humans and/or animals. They are easily spread from an infected organism to a healthy one, for which effective means and methods of treatment and prevention are available, including vaccines.

This group is subdivided into pathogenic biological agents that causei:

- highly dangerous infectious diseases;
- infectious and/or parasitic diseases;

3. **Pathogenicity Group III** – pathogenic biological agents that cause infectious and/or parasitic diseases in humans and/or animals or can cause significant harm to plants, characterized by minimal spread from an infected organism to a healthy one, for which effective means and methods of treatment and prevention are available, including vaccines;

4. **Pathogenicity Group IV** – pathogenic biological agents that cause infectious and/or parasitic diseases in humans and/or animals or that may cause damage to plants, generally do not spread from an infected organism to a healthy one, for which effective means and methods of treatment and prevention, including vaccines, are available.

Attenuated strains of micro-organisms that are pathogenic biological agents of pathogenicity group II are classified as pathogenic biological agents of pathogenicity group III.

Attenuated strains of micro-organisms that are pathogenic biological agents of pathogenicity group III are classified as pathogenic biological agents of pathogenicity group IV.

This classification of micro-organisms has inverse numerical significance compared to the international classification, but is identical in meaning as it divides pathogens into 4 groups according to their hazard.

2.2 Methodology of biorisk assessment. The concepts of hazardous biological material and pathogen. Specification of pathogen biohazard. Evaluation of laboratory procedures.

Risk is the probability that an adverse event associated with a particular hazard or threat will occur and the consequences of that event. Risk is the combination of the probability and the consequence. The purpose of a risk assessment is to determine the acceptability of risks and to identify strategic measures to reduce risks [17]. Risks associated with biological agents are referred to as biorisk [11, 13].

Biosafety risks are the type of biorisk that can affect humans, animals or the environment through its exposure. This type of biorisk is encountered on a daily basis by laboratory personnel working directly with biological materials.

Biosecurity risks are the type of biorisk that comes from a person with malicious intent and potential access to a hazardous material or facility. These risks are primarily associated with the theft of a biological agent, equipment or information, misuse or deliberate use of a pathogen and unauthorised access to pathogens.

The purpose of this chapter is to present a concept for deciding on the level of biological risk and detailed technical guidance on how to conduct a biological risk assessment as part of a biorisk management system.

A step-by-step biorisk management plan includes the following steps:

1. Identification of biorisks and hazards. A biorisk assessment procedure to determine the likelihood and severity of the consequences of a biorisk.
2. Selection of a control strategy and the implementation of biorisk mitigation measures.
3. Evaluation of the effectiveness of control measures in the form of internal and external evaluations.

Biorisk assessment is a subjective process based on information about the hazardous properties of the microorganism, the complexity of the planned procedures, the laboratory infrastructure, the staff qualifications, etc.; and it is important to consider as much information as possible for the risk assessment [14, 18]. It is therefore important that the biorisk assessment is conducted by a team of experienced laboratory professionals, including scientists with specialised training.

The classification of microbial hazard groups alone is not effective for determining the level of biorisk, as the pathogen hazard group can only show the possible consequences of the biorisk, but does not adequately determine the probability of the laboratory biorisk and thus does not provide an adequate basis for a meaningful biorisk assessment [1, 13].

A reliable risk assessment should be specific to a particular laboratory, situation or institution. It should be taken into account that each facility has different resources, functions, equipment, personnel capacity, traditions and capacity to use control measures. [15, 18, 19]

As risk is a combination of probability and consequence, the biorisk assessment in the laboratory will vary depending on:

- **factors affecting the consequences of biorisk:** the properties of the biological agent (e.g. its physical condition), the hosts at risk (humans, animals, the environment), and the severity of the consequences for the laboratory worker or the environment in the event of exposure;
- **factors affecting the likelihood of biorisk:** the conduct of specific laboratory processes with a biological agent, the biorisk mitigation measures used, and the qualifications of the personnel.

A risk where there are serious severe consequences but a minimal probability is very different from a risk with a high probability and minimal consequences. A risk with a high probability and severe consequences is, of course, is a high risk.

The main question in assessing and characterising biorisk is, what is the level of risk, that is it acceptable to work with?

The level of biological risk, based on an assessment of the probability and consequences of biorisk, is determined using a biorisk matrix (Tables 2, 3, 4).

Identification of biological risks and hazards

The first step is to identify the biological agents to be handled (or, if the biological agent in the sample is unknown, the presumptive agents) and to determine possible risks:

1. Risk of infection to personnel in the laboratory (laboratory workers):
   - through droplets or aerosol inhaled into the upper or lower respiratory tract (inhalation route);
   - through broken skin or direct injection into the bloodstream (the contact route);
   - through mucous membrane exposure;
   - by contact with the gastrointestinal tract (alimentary route).
2. Risk of infection to humans or animals outside the laboratory:
   - through droplets or aerosol inhaled into the upper or lower respiratory tract (inhalation route);
   - through broken skin or direct injection into the bloodstream (the contact route);
   - through mucous membrane exposure;
   - by contact with the gastrointestinal tract (alimentary route).

3. Risks of human or animal infection due to secondary exposure.

- The more detailed the definition of a possible biorisk, the more useful the information will be for making risk-reduction decisions later on.

The starting point **for determining the seriousness of the consequences of biorisk** is the identification of the dangerous biological agent. The pathogen assessment can be recorded in specific forms such as the «Pathogen Safety Data Sheet (PSDS)»; similar documents are used in the USA and Canada [20, 21].

A PSDS is a technical document that must be formally approved at the management level of the laboratory or the organization of which the laboratory is a part. This document is used by the personnel working with that pathogen in the laboratory. The PSDS must be printed and kept in the laboratory in a location known and accessible to personnel who comes into contact with the specific pathogen.

Although the PSDS shall be in the arbitrary form accepted by the laboratory, the following mandatory elements should be included in the document:

1) characterisation of the biological agent, including pathogenicity factors, infectious dose (if applicable);
2) the pathogenicity group of the microorganism;
3) the ability of a biological agent to transmit, the potential routes of transmission;
4) planned concentration and volume of biological agent/ infectious material;
5) the clinical severity of infection by the biological agent;
6) availability of effective prophylactic or therapeutic measures, emergency measures in case of an accident, including prophylactic treatment of contacts, vaccination if available;
7) stability of the biological agent in the laboratory and in the external

environment, sensitivity to temperature and disinfectants, and survival outside the host;

8) susceptibility of laboratory personnel (e.g. persons at risk);

9) host range of the biological agent (i.e. zoonotic carriers and vectors);

10) endemicity of the biological agent in the local population;

11) special precautions such as working with a genetically modified micro-organism, with a vaccine strain or with microorganisms with antimicrobial capacity, etc.

The Department of Biosafety and Biosecurity of the NSCEDI has developed a form of PSDSs for microorganisms of pathogenicity groups 1-2, which can be used for the biorisk assessment procedure (Appendix 2). The PSDS for a single microorganism may vary to account for certain biological characteristics of the strain, e.g. attenuated or vaccine strain, etc., which should be indicated on the PSDS form.

Based on the specification of the biological agent, a severity category for the subsequent biorisk assessment is determined (Table 2).

Table 2 – Categories of severity of biorisk consequences

Category	Description
Disastrous	Death or permanent total disability. Loss of ability to perform tasks. Severe adverse effects on the body, irreversible in some aspects.
Heavy	Persistent partial disability or temporary total disability resulting in sick time of less than 3 months. Significantly impaired ability to perform tasks. Significant adverse effect on the body; considerable effort to correct the harm through the intervention of specialised medical care; irreversible without this intervention and effort.

Category	Description
Medium	One or more injuries or illnesses resulting in less than 3 months' sick leave. Reduced ability to perform tasks. Negative effects on the body, reversible within a certain period, requiring specialist intervention.
Unimportant	One or more injuries or illnesses requiring first aid or medical treatment. Minor or no adverse effect on the ability to perform tasks, fully reversible in the short term without specialist intervention.

The severity category of the consequences is indicated in the form «Biorisk Assessment Act» (Annex 1).

In order to determine the probability of biorisk an assessment of the laboratory procedure is made taking into account the available control and mitigation measures in the laboratory. The biorisk with available controls is determined first, called the INITIAL BIORISK, and the biorisk after additional controls and mitigation measures are applied, is called the FINAL BIORISK.

It is important that each individual laboratory has a description of available biorisk mitigation measures such as the isolation of the contagious area of the laboratory, effective ventilation and air filtration systems, pathogen mitigation equipment (UV lamps, biosafety cabinets, individually ventilated animal cages etc.), the use of personal protective equipment, staff training on all biosafety issues including proper use of PPE and FIT testing, procedures for personnel entering into laboratory routines, etc. A detailed review of the biorisk mitigation measures will be presented in Part III 'Control Measures'.

The 'Biorisk Assessment Report' (Annex 1) shall indicate all the important biorisk mitigation measures available in the individual laboratory.

By determining the probability of biorisk as a result of a laboratory procedure, the following factors are primarily relevant:

1) planned laboratory procedures and the probability of aerosol formation with pathogenic material (e.g. centrifugation, vortexing, ultrasound treatment, aerosolisation, etc.);
2) hazardous work, such as handling sharp objects, working with laboratory animals and procedures involving large quantities of bacteriological material;
3) the competence of the staff doing the work, the availability of specific immunisations (if possible), the workload of the laboratory and of individual staff.

Traditionally, the most dangerous procedures include: opening of the culture ampoule, centrifugation, inoculation (infection) and necropsy of experimental animals, care of infected animals, transfer of viral and bacterial cultures, titration of suspended cultures of microorganisms, sampling and sampling, etc.

Thus, the factors influencing the degree of probability of INITIAL and FINAL biological risk are the methodology of the laboratory procedure; the level of qualification and training of the personnel performing the procedure; the measures available to mitigate biorisk: laboratory facilities, ventilation and air filtration systems, including negative pressure, equipment (biosafety cabinets, UV lamps); personal protective equipment used.

The pathogen exposure probability category is determined taking all factors into account (Table 3).

Table 3 – Coding of biorisk probability categories

Category	Description
Frequent	Occurs very frequently or continuously during the performance of a specific procedure or protocol
Probable	May occur as expected during the performance of a particular procedure or protocol. Occurs frequently or periodically.

Category	Description
Random	May occur during a specific procedure or protocol, but not often. Occurs a few times during the entire operation.
Rare	Not expected during the execution of a specific procedure or protocol. Occurs rarely as an isolated incident.
Unlikely	Almost impossible during a specific procedure or protocol. Occurs extremely rarely or almost never.

The categorisation of the probability of exposure to biorisk, taking into account the available control measures, is indicated in the «Biorisk Assessment Report» (Appendix 1).

Table 4 – Biological risk matrix

Severity of the consequen-ces	Probability				
	Frequent	Probable	Random	Rare	The unlikely
Disastrous	Extre-mely high	Extre-mely high	High	High	Mode-rate
Heavy	Extre-mely high	High	High	Mode-rate	Low
Medium	High	Mode-rate	Mode-rate	Төмен	Low
Unimportant	Mode-rate	Low	Low	Low	Low

Once the probability and consequences of the biorisk have been determined, a «biorisk matrix» (Table 4) is compiled to allow a determination of the INITIAL BIORISK level. It also takes into account the available biorisk mitigation measures. The whole process is needed to determine if the **biorisk is acceptable or not?**

Thus, the INITIAL BIORISK for the same laboratory procedures and with the same pathogen, BUT in different laboratories will be different,

laboratory-specific, so it will depend on the infrastructure and equipment of the laboratory, staffing capacity, tradition and functional capacity.

The biorisk characterisation allows you to determine whether the biorisk is acceptable or not. If the risk is unacceptable, mitigation measures must be taken to reduce the risk to an acceptable level.

Low-level biological risks are classified as acceptable risks and do not require the application of additional biorisk mitigation measures.

Biological risks with moderate, high and extremely high levels are classified as unacceptable risks and require additional measures to reduce the biorisk to an acceptable level.

Biorisk mitigation measures are used as basic and additional measures:

- engineering measures and equipment to isolate and decontaminate pathogens;
- administrative arrangements;
- protective clothing and personal protective equipment;
- training of staff on all biosafety issues.

It is important to identify such additional measures that will reduce the likelihood of biorisk to an acceptable level.

Finally, the Biorisk Assessment Report indicates the level of biorisk taking into account additional control measures - the FINAL BIORISK.

The biorisk assessment report is the main authorisation document for planned procedures and is signed by the person who carried out the biorisk assessment and the performers of the procedure.

Risk assessments should be carried out periodically and also when any aspect of the operating situation changes. The biorisk assessment process can be used to evaluate and test contingency plans as well as preventive maintenance plans for critical equipment and facility functions.

Find here some examples of actions or events where a biorisk assessment is required:

- new infectious agents, toxins, reagents or other dangerous substances;
- new biological models or new ways of introducing biological agents;
- a change in laboratory procedure and manipulation;
- the use of new equipment;
- changes in personnel;
- changes in the manufacturer or supplier of consumables (PPE, containers, waste materials, media, etc.);
- equipment that may no longer work efficiently because it has failed or has not been properly repaired/maintained;
- relocation or renovation work in the laboratory;
- an intra-laboratory case of contamination, pathogen theft or other biosafety/biosecurity breach;
- changes in local infrastructure (electricity, water, roads);
- national, regional or local political changes that can result in a security threat;
- results of the biorisk assessment determine the appropriate biological risk mitigation measures and biosecurity measures to achieve an acceptable or manageable level. New or modified risk mitigation measures can be introduced when necessary.

A thorough, scientifically sound and transparent risk assessment balances safety measures against the actual risk of handling biological agents on a case-by-case basis. This allows the implementation of cost-effective and sustainable laboratory biosafety measures appropriate to the context and priorities of laboratories.

By international standards, risk assessment is an important step in reducing biological laboratory risks. In many countries, the biological risk assessment procedure is a legal obligation as part of the biorisk management process or as a basis for determining the necessary risk reduction measures. Many of the leading guidance documents on

biosafety including the WHO Laboratory Biosafety Manual, the US Biosafety Manual for Microbiological and Biomedical Laboratories, the international standard CEN Workshop Agreement (CWA) 15793: 2011 - Managing Biorisk in Laboratories emphasize that risk assessment is a fundamental planning step for managing these risks [2, 3, 7, 15, 47, 48].

2.3 Roles and responsibilities for risk assessment

The biorisk assessment process is a consolidated contribution of the laboratory or institution staff and should not be managed or performed solely by the laboratory biosafety officer. The biorisk assessment procedure should be documented in an SOP or other institutional document and should necessarily include key points such as:

- recording the results of the biorisk assessment on incoming study protocols and/or SOPs, indicating «Agreed», «Not Agreed», «Sent for revision»;
- reviewing the biorisk assessment procedure, with more than one reviewer involved in cases of complex procedures, and here it is important to have a defined timeframe for the review. The reviewer should be a specialist with expertise in the issues raised in the document;
- consideration of the worst possible risk, identifying possible consequences for staff;
- consideration of conflicts of interest and risks, such as commercial, intellectual, institutional, copyright and others;
- the possibility of making a decision by voting with a large number of interested professionals, e.g. at a local biosafety committee meeting;
- mandatory reporting or other procedures for follow-up actions after the biorisk assessment, e.g. additional control measures or changes to the laboratory procedure, etc.

Consider the roles and responsibilities of all laboratory staff from management to the lowest level in assessing biorisk and generally

in ensuring, complying with and monitoring biosafety/biosecurity requirements in the laboratory.

The management of the laboratory.

The management is made up of laboratory directors and high-level managers and is normally not directly involved in the biorisk assessment process. However, laboratory management is ultimately responsible for the organization's biorisk management system and must therefore support and guide laboratory personnel in conducting biorisk assessments, allocate time and resources to implement the biorisk assessment procedure and implement appropriate control measures. Where appropriate, laboratory management shall reinforce its commitment to safe laboratory operations in the organization's biosafety policy.

It is the responsibility of laboratory management to ensure that the infrastructure and capacity for biosafety measures are in place, at a minimum, within national requirements and that adequate standard operating procedures are in place to minimise laboratory risks, provide PPE, serviceable equipment and facilities to perform the work. .

Biosafety specialists / local biosafety committee.

The Laboratory Biorisk Management designee shall be independent of Laboratory Managers and shall be responsible for the implementation of an effective Laboratory Biosafety Program. The Biosafety Specialist shall contribute to the biorisk assessment by compiling appropriate information to determine risk in terms of likelihood and consequences. The Biosafety Specialist shall work with the investigators to conduct the biorisk assessment and document the results of the biorisk assessment in the Biorisk Assessment Report, notify laboratory management of the results of the biorisk assessment. They shall be knowledgeable about laboratory activities, sources of potential exposure and means of effective control. They shall also act as advisers to recommend and implement appropriate risk mitigation measures resulting from the risk assessment. The biosafety specialist, in addition to the biorisk assessment, shall conduct an annual internal laboratory biosafety compliance audit for a continuous cycle of improvement of the biorisk

management system in the laboratory. The minimum qualification for a Biosafety Specialist requires knowledge of microbiology, experience in laboratory work with infectious material and fundamental training in all biosafety issues. A template for the Biosafety Specialist job description is provided in Appendix 3.

If there is a constant flow of research requiring biorisk assessment, the laboratory should have a local Biosafety and Biosecurity Committee whose members are generally reputable laboratory personnel, have laboratory experience and competence and/or qualifications in biological risk assessment.

If necessary, the organisation may organise a standing biosafety and biosecurity committee with established positions, instructions and responsibilities.

<u>Key researchers/scientists/researchers</u>

Initiate biorisk assessment and provide initial information and data for the biorisk assessment - this may be a new study protocol or a new SOP or changes to an existing SOP. Together with the head of laboratory, the Biosafety Specialist conducts the biorisk assessment and provides the results of the biorisk assessment and information on risk mitigation measures to management. They are also responsible for ensuring that staff involved in the study are informed of the results of the risk assessment and for training them in the necessary risk mitigation measures [3].

2.4 Practical tasks for the section

Practical exercise in section 2.2:

Familiarise yourself with the PSDS form. Think about how you would fill it out for a microorganism of pathogenicity group 1-2 (risk category classification) that you are working with.

The completion of the PSDS is performed by an expert with sufficient theoretical knowledge and practical experience with the pathogen. If a

suitably qualified expert is not available (e.g. at the start of a new research project in a laboratory), an external expert can be engaged from an external organisation. All relevant and reliable sources of information on the pathogen: articles and reviews (e.g. from the PubMed collection, http://pubmed.gov), WHO communications, textbooks should be used to complete the SOP. PSDS information from the Public Health Agency of Canada can also be used:

https://www.canada.ca/en/public-health/services/laboratory-bio- safety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html

Practical exercise 1 in section 2.3:

Imagine that you intend to start a research project to infect white mice with an avirulent strain of Yersinia pestis KIM D27. You hope to study the mechanisms of cellular immunity production in plague infection. In the available literature, you have not found any case of a healthy adult developing the disease through exposure to Yersinia pestis KIM D27. Consider whether it is necessary to complete an PSDS for this microorganism?

Practical exercise 2 in section 2.3:

Try to complete the PSDS for Yersinia pestis.

Check that your answer is correct in the «Workshop Answers» section of this guide.

When you looked at the PSDS form, you may have noticed in section II «Health risks» the term «risk group». Before we look at this concept, let's look at what risk is?

We considered earlier that there is a risk of harm to any pathogen-related activity, including storage. Risk is a measured hazard. In biostatistical terms, **risk** is the ***combination of the probability*** of harm occurring and ***the severity*** of its consequences.

What is probability? **Probability is a** quantitative measure of the possibility of an event occurring, the ratio of the number of positive outcomes to the number of trials.

If we toss a body that is heavier than air (such as a metal ball) into the air and assume that it falls to the ground as the outcome, then this outcome will **always** occur. Such an event (let's call it E) is called a credible event. The probability of **a credible event** is one. Indeed, if we toss a balloon in the air 100 times, it will fall to the ground 100 times:

$$= 1$$

A credible event can also be expressed as a percentage ($1 \times 100\% = 100\%$): 100% of a balloon toss test will result in the ball falling to the ground.

On the other hand, a balloon heavier than air will never fly upwards, regardless of the number of trials. Such an event is called **an impossible** event. Its probability is zero:

$$= 0$$

Thus, the probability of a random event E always lies between 0 and 1:

For example, if you flip a coin long enough, the probability that an eagle will fall is 50%, i.e. $P(E) = 0.5$.

Quantitative probability assessment is the most accurate, but not always the most convenient (it is not always possible, including for ethical reasons, to conduct experiments to estimate the probability of harm occurring). However, when the reasons for a possible event to occur outweigh the contrary reasons, the event is called probable, otherwise it is called ***unlikely***. The dominance of positive reasons over negative ones, and vice versa, can be of varying degrees, making probability (and improbability) either ***higher*** or ***lower***. Therefore, probability is often assessed at a qualitative level, especially in cases where a more or less precise quantification is impossible or extremely difficult. Different gradations of «levels» of probability are possible.

In practice, it is the qualitative assessment of the probability of harm that is used in biological risk assessment (Table 5).

Table 5 – Correspondence between indicative quantitative and qualitative estimates of levels of probability of harm

Quan-tification	Qualitative assessment / level	Code	Description
>50%	Frequent	A	Occurs very frequently or continuously during the performance of a specific procedure or protocol.
>10%	Probable	B	May occur as expected during the performance of a particular procedure or protocol. Occurs frequently or periodically.
>1%	Random	C	Can happen during a specific procedure or protocol, but not often.
>0,1%	Rare	D	Not expected during the execution of a specific procedure or protocol. Occurs rarely as an isolated incident.
>0,01%	Unlikely	E	Almost impossible during a specific procedure or protocol. Occurs extremely rarely or almost never.

Once again, risk is the combination of the likelihood of harm occurring and the severity of its consequences.

For example, if the manipulation of a broth culture of a certain pathogen is carried out by trained and untrained laboratory technicians, the probability of harm (spillage of the culture) will be higher in the latter case, but the severity of the harm will be the same.

On the other hand, if a researcher inhales 100 Brucella melitensis or Brucella neotomae microbial cells, the probability of microbial contamination is the same, but the severity of the harm is different: the first agent causes severe disease in humans, while the second does not cause brucellosis in healthy individuals.

In biological risk assessment practice, the following table (Table 6) is useful for a qualitative assessment of the occurrence of harm:

Table 6 – Qualitative criteria for levels of severity of harm

Degree of severity of the impact of the harm	
Level	**Description**
4	A major negative impact, irreversible in several ways, whether sudden onset or not
3	Significant negative impact only in the longer term; significant effort to remedy through specialist intervention; irreversible without this intervention and effort
2	Negative impacts, reversible over a period of time, require specialist intervention
1	Negative impacts are usually fully reversible in the short term without specialist intervention

PART III.
BIOLOGICAL RISK CONTROL AND ASSESSMENT OF THE EFFECTIVENESS OF CONTROL MEASURES

The results of the biorisk assessment determine the selection of appropriate biorisk mitigation and biosecurity measures to achieve acceptable or manageable levels. The results of a well-conducted biorisk assessment demonstrate that some biorisk can be managed with relatively simple control measures such as good microbiological practices, storage of pathogens in confined areas, use of additional PPE, etc. Controlling other biorisks may require more serious control measures, more resources, such as a HEPA air filtration system, installation of negative pressure and maximum isolation of infectious premises, a waste water decontamination system, use of respirators with positive pressure and inhalable air filtration, keeping infected animals in microisolators, etc.

This chapter will describe the biological risk mitigation or control measures used in the laboratories and the strategy for their selection and implementation.

The following groups of biorisk mitigation measures are differentiated [2, 12. 15]:

- cancelling the procedure or replacing it with alternative approaches;
- planning, engineering and installing biosafety equipment in laboratories;
- administrative and managerial arrangements for the provision of the biosafety and biosecurity in the laboratory;
- using of personal protective equipment (PPE);
- training of staff in all aspects of safe laboratory work.

Cancelling the procedure or replacing it with alternative approaches.

Eliminating or substituting a hazardous procedure implies not carrying out the intended work or deciding not to work with a particular biological agent and provides the highest degree of risk reduction. However, it is not always possible to eliminate a hazardous procedure. In such cases, replacement of the source of the hazardous biorisk with another source that poses less risk/threat than the original risk may be used. For example, a laboratory could potentially replace a strain of plague microbes used for nutrient media assessment with a less dangerous simulant strain such as a pseudotuberculosis strain that could be used for this purpose.

Biological risk reduction by design and engineering solutions include functional zoning of laboratory areas into 'contaminated' and 'clean' zones and ensuring non-intersecting flows of personnel and material, proper interior finishings, installation of supply and exhaust ventilation with filtration of contaminated air, laboratory access system and video surveillance, clear marking of laboratory space and laboratory equipment, and the installation of hygiene equipment for cleaning and disinfection. The basic laboratory biosafety equipment includes class 2 biological safety cabinets with HEPA filtered discharge air, a steam sterilizer (autoclave) for decontamination of contaminated material and medical waste, UV lamps, etc.

Administrative and managerial arrangements for laboratory biosafety include formalized regulations, guidelines, policies, standards, instructions, SOPs, orders, etc. for all biosafety and biosecurity issues, including laboratory authorization for work with biological pathogens, staff qualification and training requirements, medical waste regulations, regulations for accounting and movement of pathogens and infected samples, maintenance of work logs, labelling of facilities, and development of a Laboratory Biosafety Manual. An important aspect of administrative measures is the medical surveillance and health screening of laboratory personnel.

The use of PPE involves the provision of PPE in laboratories, the proper use and disposal of PPE and the training of personnel in the correct donning and doffing of PPE. Personal protective equipment refers to items of clothing and devices worn by laboratory personnel to protect against pathogenic hazards:

1) laboratory coats, aprons and coveralls, armbands;
2) laboratory shoes;
3) gloves;
4) eye and face protection;
5) respiratory protection;
6) head and hearing protection..

PPE is considered the least effective means of control because it only protects the person wearing it, and only when used correctly.

Training of personnel in biosafety shall include training of laboratory personnel from lower levels to professionals with advanced training in safe laboratory practices and techniques for handling pathogens. Staff training includes induction, specific certification course, periodic refresher courses, detailed job descriptions, and staff competency evaluations. For example, all staff shall be informed about the biorisk facilities available in the laboratory, how to minimise splashes and aerosols to avoid laboratory infections, how to properly handle medical waste, etc.

It should be understood that the application of these biological risk reduction measures, in addition to exclusion and substitution, reduces the likelihood of biological risk. Biological risk avoidance and substitution reduces the severity of the consequences of biological risk. Assessing risk and understanding the likelihood and consequences of different risks is important because it provides the basis for strategic decisions on control measures.

All types of control measures to reduce biorisk are important, but none is completely effective in controlling or reducing all risks. Each group of biorisk mitigation measures has advantages and disadvantages (Table 7).

Table 7 – Measures to reduce biological risks

Control measures	Advantages	Disadvantages
Engineering	Effective, eliminates danger	Expensive, complex
Administration and management	The authority-based approach	The indirect approach is primarily aimed at the human factor
Good practices and procedures	Based on the SOP (standardised approach) and training programmes	Staff training and supervision needs
PPE	Easy to use, relatively low cost	Do not eliminate danger, PPE does not help in case of contact, uncomfortable, limits ability

The most effective control measures include engineering measures, the least effective in reducing biorisk is personal protective equipment [2, 12].

In practice, the laboratory should use a combination of control measures **according to the principle of greatest efficiency and economic sustainability**. The use of expensive engineering measures is not reasonable for low biohazard procedures. For example, HVAC ventilation systems with HEPA air filtration require highly skilled engineers, equipment maintenance and an annual supply of expensive HEPA filters. If the laboratory does not have sufficient funds to operate the HVAC system year-round, as well as the funds required for periodic testing and replacement of HEPA filters, this approach will not be sustainable and the resources used will be a waste of time and finances and ultimately fail to reduce biorisk. In this case, a more sustainable approach would be to use fine air filters with consideration for laboratory procedures in class 2 biosafety cabinets.

On the economic side, the most effective and cost-effective measures are administrative measures and training of staff. Of the engineering

measures, an effective and economically sustainable approach is the zoning of the laboratory with separation of the air space into «clean» and «infectious» zones, the use of biological safety cabinets as equipment for the primary isolation of the pathogen.

The laboratory needs to develop a biorisk control strategy for specific nosologies, taking into account the planned procedures. A greater responsibility in deciding on a strategy for biorisk mitigation measures lies with the persons who must assess the control measures and resources already available, staff knowledge and competences, and propose additional adequate measures to ensure that the biorisk is acceptable.

Thus, the principles for selecting and implementing biorisk control measures should:

- use a combination of several risk control strategies;
- select and use the measures that are available and most sustainable, including those that are economically sustainable;
- rely primarily on national regulations requiring prescribed risk controls [6, 8, 9, 10, 45];
- ensure that the residual risk after the application of additional control measures to reduce biorisk moves into the acceptable risk category.

3.1 Engineering measures and equipment to reduce biological risks

It is ideal if the laboratory designs and implements biorisk mitigation engineering measures in advance, taking into account the planned studies with microorganisms of pathogenicity groups I-IV.

The planning stage of the laboratory is the most important stage for the installation of basic engineering measures to reduce biological risks, as the implementation of engineering systems already in operation will require significant adjustments to the existing building infrastructure and will be associated with significant financial and time resources.

When planning the laboratory and the necessary engineering systems, the following points must be clearly understood:

1. What is the main functional purpose of the laboratory: diagnostic, production, research, education, testing, pathogen depository, etc.?

2. Which micro-organisms will be used in the laboratory, hazardous, non-hazardous, micro-organism pathogenicity group?

3. What types of tests will be carried out: bacteriological, immunological (ELISA, IIFA), microscopic, molecular genetic (PCR), etc.?

4. How much testing will the laboratory do on a daily, monthly, quarterly basis?

5. Will there be a vivarium in the laboratory for experimental animals for biomedical research and which biological models are planned to be kept in the vivarium?

6. What will be the basic layout of the rooms: a one-corridor or a two-corridor layout? What kind of airlock will be installed between the clean and infectious areas?

7. What basic equipment and how many pieces of equipment will be in the laboratory: biosafety cabinets, autoclave, laboratory equipment, animal isolators, low temperature refrigerators?

8. What secondary equipment will be in the laboratory: washing equipment, protective and personal clothing cupboards, medical waste containers, refrigerators, cleaning mop equipment, shelving, antibacterial mats, etc.?

9. What engineering systems will be installed in the laboratory building: ventilation and air filtration system, security systems and controlled access to the laboratory, water filtration system, automation of equipment and engineering systems, fire alarm and notification, communication, light control, video surveillance, etc.?

Based on such data, a conceptual laboratory design is initially developed, where the lab layout indicates the zoning of the rooms

into 'clean' and 'contaminated' zones, how the equipment and main laboratory furniture are arranged, airlocks, location of transfer windows, sinks, lift, all doors, including which way they open, and all other important engineering and technological solutions are specified. Secondary details such as emergency source of electricity, built-in furniture, storage and washing equipment and much more should not be forgotten.

When choosing a layout, consider the disadvantages and advantages of each option:

One-corridor layout:

Disadvantages: high likelihood of cross-contamination, increased cleaning costs, the need for clear administrative planning of the laboratory, high staff commitment.

Advantages: easy adaptation of existing traditional spaces, fewer ancillary areas, less duplication, cheaper construction.

Two-corridors layout:

Disadvantages: extensive renovation of the premises, more ancillary areas, higher ventilation load, more duplication, higher construction costs.

Advantages: Reduces possibility of cross-contamination.

During the conceptual design phase it is necessary to have the advice of a group of relevant experts, both building professionals and laboratory organisers. It is very important at the conceptual design stage of the laboratory to determine the economic feasibility of the laboratory, i.e. what costs are expected by the laboratory (especially energy and water consumption) during its operation and how the laboratory will justify them. Do not forget about the public and social benefit of the laboratory to the surrounding community. Subsequently, based on the conceptual design, design and estimate documents are prepared to determine the full laboratory construction budget and the equipment to be purchased. Further, continuous project management and author's supervision of compliance with the design and estimate

documentation is required during the construction of the laboratory. Of course, if necessary, the necessary renovation engineering systems can already be installed in the existing laboratory.

Laboratories shall be provided with water supply, sewerage, electricity, heating, telephone/internet, as well as security and fire alarms. The laboratory shall be provided with fire extinguishing equipment.

A laboratory handling dangerous pathogens (pathogen group I-II) shall be equipped with induced-draft ventilation with fine filters (HEPA filters if necessary) at the outlet. Air filtration can also be provided on the supply side, but from a biosecurity point of view, this is not necessary and would require additional resources for periodic replacement of the supply filters. For a supply and exhaust system, there must be separate ducting for supply and exhaust, with diffusers in each room. For a supply and exhaust system, a separate ducting system for the supply and for the exhaust with diffusers in each room must be provided. The ducting of the supply and exhaust systems is recommended to be made of galvanised steel resistant to disinfectant, the casings of the supply machines should be made of stainless steel. The capacity of the air inlets must be proportionate to the ventilated air volume with an excess of 1.5 times. Provide exhaust air treatment in the form of a 2-3 stage filtration:

- F5-F9 fine filters on the extractor hood, install H10-H14 HEPA filters if necessary (e.g. a combination of F5-H10 filters);

- if necessary, rough filters G1-G4 and fine filters F5-F9 (e.g. a combination of G3-F7) on the inflow. To prevent the risk of aerogenic contamination, exhaust shall prevail over inlet and if necessary, create negative pressure in the pathogenic laboratory areas with a static pressure differential of 3-5 Pa between rooms in the contagious area and 15-30 Pa between rooms in the contagious and clean areas. The air exchange rate in laboratory rooms is 10-12 times per hour, with a flow velocity of no more than 3 m/s. Provide a periodic schedule for the safe replacement of contaminated filters. **Important:** Replacing contaminated

filters is a high biohazard activity and must only be carried out by trained engineers.

If necessary, provide an automated ventilation system with the ability to monitor and control the following options: temperature and humidity control, differential room pressure, air exchange rate and airflow rate. Such a ventilation system is called a HVAC system and is installed in BSL-3 / BSL-4 laboratories and has to be validated by external specialists.

For laboratories handling pathogens of groups III-IV of pathogenicity, the 'contagious' area shall be minimum equipped with a supply and exhaust ventilation with artificial inducement without filters.

For laboratories handling pathogens of groups III-IV of pathogenicity of the district level, mechanical induced ventilation is allowed.

Air filters are divided into 3 classes of filtration efficiency (filtering capacity): G1-G4 for particles larger than 10 μm, F5-F9 for particles larger than 1 μm and H10-H11 for «absolute» HEPA filters. Also, ultra-high-purity (ULPA) filters are sometimes identified as a separate class.

The classification of air filters is shown in table 8 [22]:

Table 8 – Classification of air filters

Degree of cleaning	Cleaning class	Trapped particles and applications
Rough	G1	Coarse filters used in rooms and processes with low air purity requirements. Pre-cleaning in ventilation and central air conditioning systems. Used for compressors, refrigeration machines in dusty environments. Detains large particles such as down, soot, coarse dust particles, insects, feathers, and large plant seeds. Cleaning efficiency of 60-90%.
	G2	
	G3	
	G4	

Slim	F5	Fine air filters in air conditioning and ventilation systems. Purification of cycle air of gas turbine units. Used as second stage filters (aftertreatment). Used in hospital wards, laboratories, administrative buildings, hotels, food and pharmaceutical production, electronics, meat and dairy industries, etc. Retains particles larger than 1 micrometre: fine dust, fluff, fine plant pollen, fungal/mould spores, bacteria. Up to 95% cleaning efficiency.
	F6	
	F7	
	F8	
	F9	
High efficiency (HEPA)	H10	Absolute filters are used for clean areas, clean rooms, in the pharmaceutical and electronic industries, for sanitation, hygiene and microclimate areas in hospitals (operating theatres); in nuclear power plants; in food production (fermentation rooms), pharmaceuticals, etc. Retains particles larger than 0.3 micrometres: the smallest highly allergenic dust, fungal spores, pollen, hazardous viruses and bacteria, and smog particles. Up to 99.99% cleaning efficiency.
	H11	
	H12	
	H13	
	H14	
Ultra high performance (ULPA)	U15	Final air cleaner for rooms with the highest requirements for air purity. The filtration efficiency ranges from 99.9995% to 99.9999995%.
	U16	
	U17	

The laboratory shall be equipped with a redundant power supply system and an autonomous (reserve, emergency) power supply (diesel generator), which must ensure uninterrupted operation of important engineering systems and equipment, necessarily an air ventilation system!

In accordance with Kazakh regulatory requirements the laboratory [8, 9, 18] where the pathogen is handled shall be located in a freestanding building or in an isolated part of the building with an independent entrance. The laboratory entrance door must be marked with the name of the laboratory and the biohazard sign (Figure 2). The entrance door must have a locking device and access to the laboratory shall be restricted to authorised personnel. Internal doors shall be labelled with the functional name of the room.



Figure 2 – Biohazard sign

Laboratories carrying out diagnostic tests shall be equipped with two entrances, one for staff members and one for the receipt of diagnostic/ biological material. Material may be received through a transfer window or a transfer sluice.

Laboratory can be divided into a 'contaminated' and a 'clean' area, with an airlock between them for changing protective clothing and taking showers if necessary. The zoning of the laboratories should ensure that the flow of both infected material and personnel does not overlap. All doors in the 'contagious area' should be equipped with door closers.

The main purpose of the airlock with a sanitary passageway is to prevent pathogens from escaping from the contaminated area on the clothes and shoes of personnel and other contaminated objects. The airlock has self-closing sealed doors and, if necessary, an interlocking device is installed in the airlock to prevent both doors from opening at the same time.

The «contaminated area» of the laboratory shall include the following set of sequentially arranged rooms and/or separately identified work areas within other functional areas:

The «clean» zone must have the following facilities:

1. Staff entrance and cloakroom for street clothes.
2. Premises for putting on a medical suit/pyjamas (male/female).
3. Warehouse.
4. Document workrooms.
5. Toilet (male/female).
6. Rooms for preparatory laboratory work.
7. Sterilisation room and/or «clean» autoclave.
8. A room for the preparation and dispensing of nutrient media.
9. Washbasins.
10. Storage room for cleaning equipment for the clean area.
11. An airlock between the contagious and clean areas with a sanitary passageway (male/female).

The «contagious» zone must have the following facilities:

1. Decontamination autoclave (if possible, install a walk-through autoclave between the 'contagious' and 'clean' areas).
2. Place/area for donning a protective suit.
3. Place/area for removing the protective suit (protective suit can be removed in the dressing room).
4. A bacteriological or virological laboratory with a dressing room – there may be more than one.
5. A virology laboratory with a changing room – there can be more than one.
6. Immunology laboratory with dressing room
7. Microscopy room

8. Room for to produce the master mix (PCR step 2).
9. PCR amplification room (PCR step 3).
10. Room for DNA/RNA isolation (PCR step 1).
11. Room for receiving and recording infected material and pathogens.
12. Parasitological laboratory with changing room.
13. Room for storage of cleaning equipment for the contagious area and preparation of disinfectant solutions.
14. A contaminated field material reception area (often an experimental vivarium for infected animals)::
    - 1 типті қорғаныс костюмін киюге арналған бөлме;
    - room for donning a type 1 protective suit;
    - type 1 protective suit removal room;
    - room for receiving and recording field material;
    - room for infestation of bio-tested animals;
    - necropsy room;
    - bio-testing animals room.

Theoretically, rooms in the infectious disease unit for receiving field material can be combined if there is no breach of biosafety.

This list above is the most complete set of laboratory facilities. Each laboratory plans a list of rooms according to the functional purpose of the laboratory, and some rooms may be missing or may be added.

The master mix room (PCR step 2) room is located as far away from the first and third steps of the PCR as possible. Each PCR area has its own set of furniture, refrigerators/freezers, laboratory equipment, reagents, automatic pipettes, tips, plastic and glassware, protective clothing, shoes, disposable gloves, cleaning equipment and other consumables used only in that room; no transfer of equipment, consumables, reagents, gloves, gowns from one area to another is allowed.

Class 2 biological safety cabinets should be installed in the bacteriological, virological, immunological laboratories, material reception and registration room and PCR step 1 room.

Modern planning approaches are available: 1) Doors in the contagious area should have sight-glasses and open inwards towards the lower pressure side of the room, 2) doors in the disinfection and washing department should have swing doors with automatic door closers, 3) only controlled artificial lighting in contagious rooms, 4) horizontal bumpers and vertical protection corners on the walls in the corridors should be installed, 5) floors in contagious rooms shall be poured of sturdy material (epoxy and polymer), 6) corner joints like wall-wall, floor-wall, ceiling-wall shall be made as rounded studs with diameter of 5-10 cm for effective disinfection and cleaning, 7) the wall between contagious and clean zones shall contain a disinfection chamber for the disinfection of large equipment (carts, cleaning equipment, racks for animals, etc.), 8) sealed fixtures to protect the unit from the disinfectant solution (minimum degree of protection IP54), etc.

Separate room for temporary storage of class B, C and D medical waste must be available in the laboratory or on the laboratory premises, equipped with a sink with hot- and cold-water supply, exhaust ventilation with mechanical inducement, scales, refrigeration equipment, shelving, UV lamp and large volume mobile containers.

There may be a separate breeding facility for special pathogen free laboratory animals (Animal Breeding facility) to provide the laboratory with biological models.

For an example, here is a diagram of the anti-plague laboratory where diagnostic tests with the plague pathogen are carried out (figure 3).

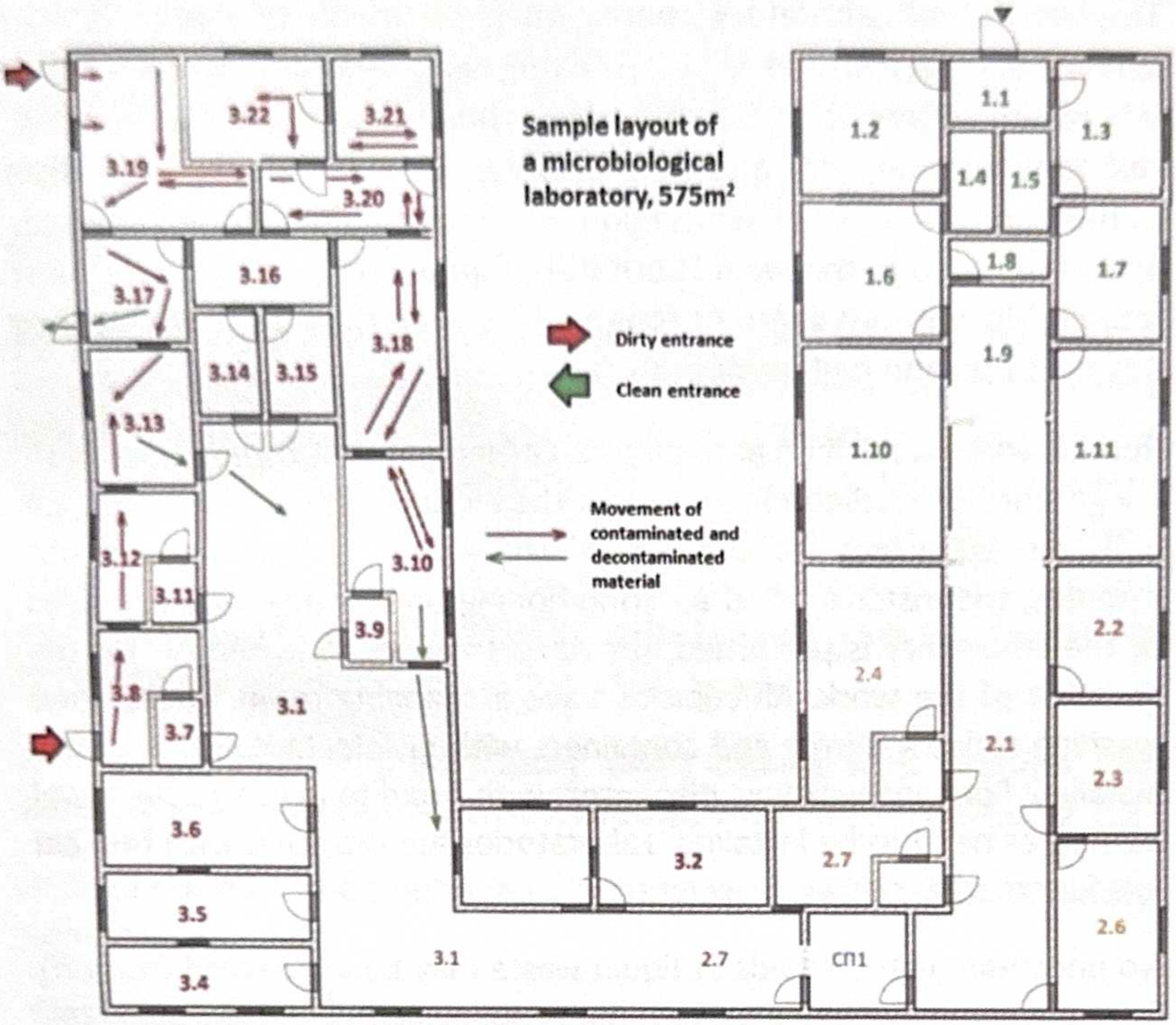


Figure 3 – Schematic diagram of an anti-plague laboratory in the Republic of Kazakhstan.

Explanation of rooms: «CLEAN» ZONE: 1.1 Entrance corridor; 1.2 and 1.3 Cloakroom for outerwear (male/female); 1.4 and 1.5 Toilets (male/female). 1.6 and 1.7 Cloakroom for protective clothing (male/female); 1.8 Utility room for cleaning equipment for «clean» zone; 1.9 Corridor; 1.10 Administrative office; 1.11 Laboratory manager's office; 2.2 Warehouse; 2.3 «Clean» autoclave; 2.4 Sterilization room; 2.5 Washroom, lab transfer window is installed between room 2.5 and 3.2; 2.6 Medium preparation room; «CONTAGIOUS» ZONE: СП1 Locker room with shower; 2.7 PPE dressing room; 2.8 Toilet; 2.9 Utility room for cleaning equipment; 3.0 PCR room for master mix preparation; 3.2 Autoclave for contagious material; 3.3 Serological testing box; 3.4 PCR room for amplification and detection; 3.5 ELISA room; 3.6 Sample preparation room; 3.8 Room for receiving, registration of cholera and clinical samples; 3.10 Bacteriological laboratory; 3.12 Bacteriological laboratory; 3.13 Serological laboratory; 3.14 PPE dressing room;; 3.15 PPE removal room; 3.17 Decontamination room; 3.18 Zoological-parasitological box; 3.19 Room for receiving and primary processing of field material; 3.20 Necropsy room; 3.21 Room for contamination of lab animals; 3.22 Room for holding infected lab animals.

The interior of laboratory rooms must be made of materials that can be disinfected and cleaned. Floor, wall, and ceiling surfaces in laboratory rooms must be smooth, without grooves, easily handled, resistant to detergents and disinfectants, and not slippery. The edges of the floor coverings of «contagious» rooms should be raised upwards and embedded in the wall. Laboratory equipment and furniture must be durable, without sharp or rough edges, waterproof and resistant to disinfectants and high temperatures.

Rooms where work with pathogens is carried out shall be equipped with UV germicidal irradiators to disinfect the air and surfaces in accordance with the guidelines for the use of UV germicidal radiation. In hot climates, the installation of air conditioning units in the working areas of the laboratory is permitted, provided they are switched off for the duration of the work. All cubicles have a changing room where hand washing sinks, a mirror and containers with disinfectant solutions are installed. For hand washing, dispensers with liquid soap and paper towel structures need to be installed. Laboratories are provided with first aid kits for emergencies and accidents.

No uncontaminated liquids or liquid waste may be discharged (run off) from the communicable area into the sewer system.

To ensure biosecurity, the area of the laboratory working with dangerous pathogens must be fenced, no unlocked doors, gates, or breaches or damage are allowed in the outer fence. Lighting shall be installed around the perimeter of the fence. Window openings on the ground floor of the laboratories shall be protected by metal grilles (sliding, swinging) or blinds of appropriate strength, and equipped with insect screens. If necessary, access to the area is controlled by a permit regime and video surveillance.

In the previous WHO Manual 2004, 3rd edition, laboratories were divided into biosafety levels (BSL-1, BSL-2, BSL-3 and BSL-4) according to the nomenclature of the laboratory, the availability of certain infrastructure and engineering solutions and other control measures. In this respect, maximum containment laboratories were classified as BSL-3 or BSL-4 for hazardous pathogens; BSL-1 and BSL-2 for non-

hazardous and moderate pathogens. Currently, the differentiation of laboratories into biosafety levels is not recommended and the individual laboratory biosafety status is based on a high-level biological risk assessment for laboratory procedures.

Biosafety equipment

Biosafety cabinets are the primary pathogen containment equipment to reduce or eliminate pathogen contact with laboratory workers and the environment and provide a safe working environment for pathogens, aerogenic viruses, cytostatics, etc. A biological safety cabinet is an equipment with laminar airflow in the controlled working area and disinfection of circulating air from suspended particles and aerosol particles by HEPA-filtration, where protection is ensured for the material, the operator and the environment.

A biosafety cabinet is mandatory when dealing with airborne and aerosolborne pathogens such as tularemia, brucellosis, SARS-CoV-2, etc.

A distinction is made between class I, class II and class III biosafety cabinets:

Class I Biosafety cabinet – protects the operator and the environment when handling hazardous agents and prevents cross-contamination inside the working chamber. The principle of operation is based on forced removal of hazardous substances from the working area by a laminar upward flow of air. The laminar flow is directed from the operator into the workspace, then purified through HEPA filters and fully extracted into the external environment. Class I cabinets are suitable for handling of materials that do not require protection.

Biosafety Class II cabinet – provides protection for the operator, the product and the environment when working with pathogenic agents and microorganisms of pathogenicity groups I-IV, when working with toxic chemicals. A Biological Safety Class II cabinet is a box with a front window through which the operator can manipulate inside the box, designed to protect the operator while minimising the risk of product contamination and cross-contamination. Downward laminar

airflow removes exhaust air through a highly efficient HEPA filter into the environment. Biosafety class II safety cabinets are divided into two types:

- type A – for work with pathogenic material in medical, bacteriological and virology laboratories; here forced air recirculation (70%) in a closed volume through a HEPA filter;
- type B – for handling pathogenic material and chemicals in medical, pharmaceutical and other facilities; no air recirculation in the working chamber, 100% exhaust air. Since chemicals cannot be filtered out and may cause harm to the operator if released into the laboratory environment, the cabinet is connected to the general ventilation system where the air is discharged.

Biosafety Class III cabinet – provides protection for the operator, the product and the environment when working with highly dangerous microbiological material, viruses, bacteria, microorganisms of pathogenicity group I, chemicals requiring atmospheric control, radioisotopes, carcinogens when assembling electronic components, and in pharmaceuticals, forensics and organic synthesis. A Biological Safety Class III safety cabinet is a cubicle in which the working area is completely isolated from the outside environment and the operator is separated from the workplace by a physical barrier and can only perform manipulations in the working chamber of the cubicle through gloves mechanically connected to the cubicle. The filtered air is constantly supplied to the cubicle and the exhaust air, cleaned by at least double HEPA high efficiency filters, is discharged through the exhaust system to the outside environment.

The most suitable option for a microbiological laboratory carrying out diagnostic and research work with pathogenic material, including dangerous pathogens, is a biosafety cabinet class II, type A.

Class II (laminar flow) biosafety cabinets must be located outside the main employee routes and also outside air currents which may interfere with the insulation provided by the air curtain in the working aperture. Windows, if any, must be kept closed at all times in the laboratory. It is recommended to leave at least 8 cm clearance on the sides of

the enclosure and 4 cm behind the enclosure and 30 cm clearance between the top of the enclosure and the ceiling. An electrical socket for powering the cabinet should be located in an accessible position so that the cabinet cannot be moved. It is important to understand that biosafety cabinets, as equipment which filters large volumes of air, must be located in closed, clean, refurbished rooms, which will extend the service life of the HEPA filter by several decades. Otherwise, e.g. with open windows, working in dusty polluted rooms, the filters will fail quite quickly and require replacement, which is almost impossible, especially in countries where biosafety cabinets are not manufactured.

The annual biosafety cabinet certification [8, 23, 24] confirms the isolation of the pathogen within the biosafety cabinet and consequently the protection of personnel, the environment and the protection of the product (for classes II and III). The following physical tests are performed as part of the certification:

- checking the downstream velocity profile;
- check the speed of the incoming flow;
- checking the smoke pattern of the air currents;
- testing of HEPA filters for leakage;
- checking the structural integrity of the enclosure (A1 enclosures only);
- checking the installation of the enclosure in the laboratory room.

In addition, the following tests can be carried out to ensure the comfort and safety of operating personnel (on request): illumination test, vibration test, noise and current leakage test, earth resistance and polarity test.

A document certifying that the biosafety cabinet has successfully passed the annual certification test shall be kept in a visible place.

Autoclaves (steam sterilisers) are used in laboratories to sterilise liquids, culture (nutrient) media, instruments, utensils, tips, pipettes, medical and biological waste, PPE, and other contaminated laboratory items by exposing them to high pressure saturated steam at temperatures from 120°C to 132°C.



Figure 4 - Vertical and flow-through autoclaves (from left to right).

Autoclaves differ in shape, volume and construction: Vertical, horizontal, flow-through, rotary, and columnar (figure 4). But all have the same structure:

- the inside is a sterilisation chamber where the objects to be treated are loaded;
- the middle part is the steam chamber where water is poured in and then heated to a vapour state. It communicates with the internal sterilisation chamber by means of openings for steam flow;
- the outer part – the casing - protects the steam chamber from mechanical influences and prevents personnel from coming into contact with the hot boiler walls.

The following advantages of the autoclave, can be highlighted:

- the high efficiency of the sterilisation procedure, the steam released easily penetrates the deepest layers of the material and completely destroys all micro-organisms;
- high reliability of modern autoclaves. Only modern, high quality materials, such as stainless steel, are used in their manufacture and automatic operation is set;
- modern technological solutions ensure economical use of water and energy.

Install the steam steriliser at 0.8 metres from the walls and the cabinet sterilisers at 1.5 metres. The floor of the room must be covered with non-conductive material and the room must be ventilated. The operating instructions shall be posted in a visible place. As the autoclave is a pressure equipment, it requires constant maintenance.

To control sterilization of the material by autoclaving, chemical indicators are used for the appropriate temperature regime: 132°C for spore-forming microorganisms and 120-122°C for non-spore-forming microorganisms. The indicators are placed each time the autoclave is loaded into the control points located at different levels of the chamber (top, bottom, centre, loading door); the number of indicators varies with the volume of the autoclave (from 5 to 15 indicators) [8, 25, 33]. Monthly bacteriological control of steam sterilization by autoclaving is also carried out using bacteriological indicators, which are spore forms of test microorganisms (e.g. Geobacillus stearothermophilus). The principle of the method is to kill the test microorganisms at a temperature of 132°C and an exposure time of more than 15 minutes.

In accordance with Kazakhstan regulatory requirements, germicidal UV lamps must be installed in bays where pathogenic material is handled to disinfect air and surfaces [8, 25]. The disinfecting effect of the UV lamp is due to the bactericidal effect of the short wavelength of 200 –315 nm emitted by the lamp. Important: Such waves can damage human skin, which staff should be aware of and take preventive measures – do not expose exposed skin to the direct rays of the UV lamp! It is obligatory to keep a record of the operating time of each illuminator and make notes in a notebook, logbook, paper or online form, etc. Operating time of the UV lamp is different for each lamp and may vary from 500 hours to 12 thousand hours, so it is best to keep records by subtracting the operating time of the lamp from the operating time specified in the data sheet. A distinction is made between wall-mounted, floor-mounted mobile, indoor and outdoor UV lamps with different sizes, configurations and operating times. A modern approach does not recommend the installation of UV lamps in rooms where personnel work, but only in small closed spaces, e.g. in a biosafety cabinet or disinfection chamber. And air disinfection is ensured by a ventilation and air filtration system.

Existing refrigeration equipment (refrigerators, freezers) must be provided with thermometers to record the temperature inside the refrigerated compartment on a daily basis (notebook, magazine, paper or online form, etc.). If there is a freezer compartment, a second thermometer is also needed to record the temperature on a daily basis.

Depending on the range of tests to be carried out, the laboratory may have the following equipment: centrifuges, thermostats and CO2 incubators, PCR equipment, ELISA equipment, vortexes, shakers, water bath, biochemistry analysers, densitometer, haematology analysers, spectrophotometers, microscopes, histology equipment, chromotograph, pH meters, lyophilisers, scales, distillers, inactivators, microincinators, dispensers, vivarium equipment and more.

All equipment, instruments and measuring devices used in the laboratory shall be in good working order, have a technical certificate and working instructions for operation taking into account safety requirements, and undergo annual certification and calibration [24, 26, 26]:

- autoclave – annual calibration of the pressure gauge;
- biosafety cabinet – annual certification;
- thermometers – annual calibration;
- drying cabinet – annual checking of the pressure gauge;
- scales, pipettes, pH meters – annual calibration.

3.2 Biosafety and biosecurity administrative measures and management decisions

Laboratory biosafety administrative and management controls include formalized regulations, guidelines, policies, standards, instructions, SOPs, orders, etc. for all biosafety and biosecurity issues. This group of control measures depends entirely on the organizational and administrative capacity of the laboratory management level. It is one of the effective measures to reduce biorisk when applied correctly and optimally, as it primarily affects the human factor, the staff. Administrative measures regulate important areas in terms of

biosafety, such as rules for accounting, movement of pathogens and infected samples, emergency response and for handling medical waste.

Consider what fundamental biosafety and biosecurity documents a laboratory should have:

1. A laboratory biosafety and biosecurity policy where management the declares, that it is responsibly that biosafety and biosecurity requirements (if applicable) are met and monitored.
2. A Biosafety Manual/Programme (see Part II).
3. The organisation's medical waste management programme (often part of the biosafety manual).
4. Contingency and emergency response plans, which include an elaborate warning system, a plan for dealing with deliberate (threat of removal, actual removal or theft) or unintentional (accidental release, fire, earthquake) situations (often part of the biosafety manual).
5. Safety and health instructions. A safety training log book for all laboratory staff.
6. Statute and composition of the biosafety and biosecurity commission (or committee).

Important administrative measures controlling biorisk are orders, permits, regulations and job descriptions approved by laboratory management. The most important of these are:

- authorisation to work with microorganisms of pathogenicity groups 1-4, issued by a state authorised body for 5 years for different types of activities (diagnostic, research and experimental, depositary, production);
- laboratory regulations specifying the scope of testing and the appropriate biosafety requirements;
- biosafety specialist job descriptions;
- staff job descriptions with a mandatory biosafety clause;
- an order for personnel authorisation to work with micro-organisms of pathogenicity group 1-2;

- an order for personnel to be allowed into certain laboratory areas;
- an order on the person responsible for controlling medical waste management;
- an order on the person responsible for the operation of ventilation and air-conditioning systems and the implementation of the schedule of preventive maintenance of ventilation systems;
- a contract for the disposal of medical waste;
- equipment maintenance agreements (verification, certification, validation/verification, etc.).

The laboratory should have a comprehensively written health and safety guidance for the workplace:

- personnel records (training, immunisations, work-related injuries and illnesses);
- informing about potential hazards in the workplace;
- developing a safe working style;
- safe operation and maintenance of equipment;
- local legislation on occupational hazards;
- health and safety instructions and instruction logs.

All routine work in the laboratory shall be regulated in Standard Operating Procedures (SOPs) developed by the laboratory staff and approved by management. SOPs shall be available in the laboratory at the workplace either in hard copy or electronically so that they can be easily opened and read. Implementation of the SOP is a part of the Quality Management System (QMS) of the Laboratory. Compliance with biosafety and biosecurity requirements is also an important component of the QMS.

The SOP programme includes general SOPs, on personnel, on laboratory procedures, on biosafety, on biosecurity, on engineering systems and equipment, on archiving rules.

A minimum list of SOPs on biosafety and biosecurity includes:

1. Entry/exit from the laboratory, including through a checkpoint (if necessary), access to contaminated and clean rooms, reception and clearance of visitors.
2. Use of protective suits and PPE in laboratory (description) in clean and contaminated areas. Places to put on, take off and store PPE. Procedure for decontamination of protective clothing.
3. Medical waste management scheme (Class A, B, C and D).
4. Cleaning and disinfection in laboratories (clean and contaminated areas, cubicles, laboratory utensils, waste).
5. Monitoring the operation of the decontamination autoclave.
6. Monitoring the operation of UV lamps and refrigeration equipment.
7. Principles of the Biological Safety Cabinet, staff briefing.
8. Receiving and processing, registering samples.
9. Rules for recording, handling, storage and destruction of microbial strains.
10. Regulations for the transport of microbial strains and biological materials.
11. Training requirements for staff on all biosafety issues.
12. Emergency and contingency plan for the laboratory (fire, flooding, etc.)
13. Conducting in-laboratory controls [8, 24].
14. Work in the field, if necessary (protective clothing, equipment and consumables, documentation, transport of field samples, rules of conduct in the field).

It **is important** that staff is familiar with the SOPs and comply with them! For this purpose, staff competence is periodically assessed, usually during an internal audit of the laboratory [26].

The procedure for developing a new SOP or revising an existing SOP, its approval and use can be organized in different ways, usually the person responsible is a QMS specialist. For example, at the NSCEDI the SOP revision is as follows: a new developed SOP (or revised old SOP) is submitted to the NSCEDI Biosafety Commission for review, if the review is positive the SOP is assigned a number (or a revision

number is entered), the SOP is approved by management, placed in the electronic cloud and the laboratory staff is familiarized with it.

The laboratory maintains a large number of records in journals, forms, records, etc. Journals are one of the common forms of records; journals shall be numbered, sewn, signed and stamped.

The minimum list of journals according to Kazakh requirements includes:

1. Personnel documentation folder (general list of employees with data, training certificates, CVs, etc.).
2. A folder or log with the inspection reports of the Regime Commission, sanitary and epidemiological services, veterinary inspections, environmental inspections and other inspections.
3. Biosafety and biosecurity briefing log for all staff and visitors.
4. Safety briefing log.
5. A register of visitors to the AOI laboratory.
6. The laboratory accident and emergency logbook.
7. Logbook for sterilisation control of steam and air sterilisers (autoclaves), including bacteriological control, indicating temperature control.
8. The temperature log of the refrigeration equipment (usually separately for each refrigerator).
9. A logbook for the operating hours of UV germicidal irradiators (usually separately for each germicidal lamp).
10. Journal for decontamination of waste material.
11. Logbook for the daily registration and deposit of medical waste in the laboratory.
12. Journal for decontamination of protective clothing and PPE.
13. Logbook for the calibration of equipment (scales, pipettes, pH-meters, etc.).
14. Cleaning log in the laboratory.
15. The internal laboratory disinfection quality control log (wipes), the objects subjected to bacteriological control and the examination procedure are presented in MoH Order No. 59 [24].

16. The logbook for intralaboratory air monitoring, the test procedure is presented in MoH Order No. 59 [24].
17. A contagious material flow log or a thermostat log (if necessary).
18. Staff temperature log (in laboratories where Group 1 pathogenicity micro-organisms are handled).
19. A logbook for samples received for testing (if necessary), each sample is assigned a laboratory number (unique code).
20. Register of cultures received for research (if necessary).
21. Logbook for the destruction of biomaterials, microbial strain cultures (if necessary).
22. Logbook on the movement of museum crops (if necessary).
23. Logbook for microbiological tests for anthrax (for anthrax laboratories only).
24. Register of bio-sampled animals of the infectious disease unit (if applicable).
25. A log of the environmental parameters of the production premises (measurements of illumination, temperature, humidity, noise, water analyses, etc.);
26. Maintenance log for laboratory equipment, to be completed by the engineers;
27. Folder with certificates and instructions for use of disinfectants, calibration certificates for autoclaves, thermometers, manometers, pipettes, nutrient data sheets, etc.

Ideally, the laboratory file nomenclature should be aligned with the relevant SOPs and journals [24, 26].

The Republic of Kazakhstan has serious requirements for the accounting, handling and transport of pathogenic agents and infectious material (8, 24).

The entire strain cycle is recorded in special logs and forms – isolation/ entry, movement, release, destruction [6, 8, 36]. A strict inventory of pathogens is maintained and their movement monitored.

Transfer of microorganisms within the organization between laboratories shall be done in sealed primary containers, vials, tanks, etc. with formal management approval. When unpacking the material,

the box, containers and test tubes shall be treated with disinfectant.

Transport of pathogens and infectious material outside the laboratory is performed according to the «triple-packaging» principle (Figure 5) [8, 27]:

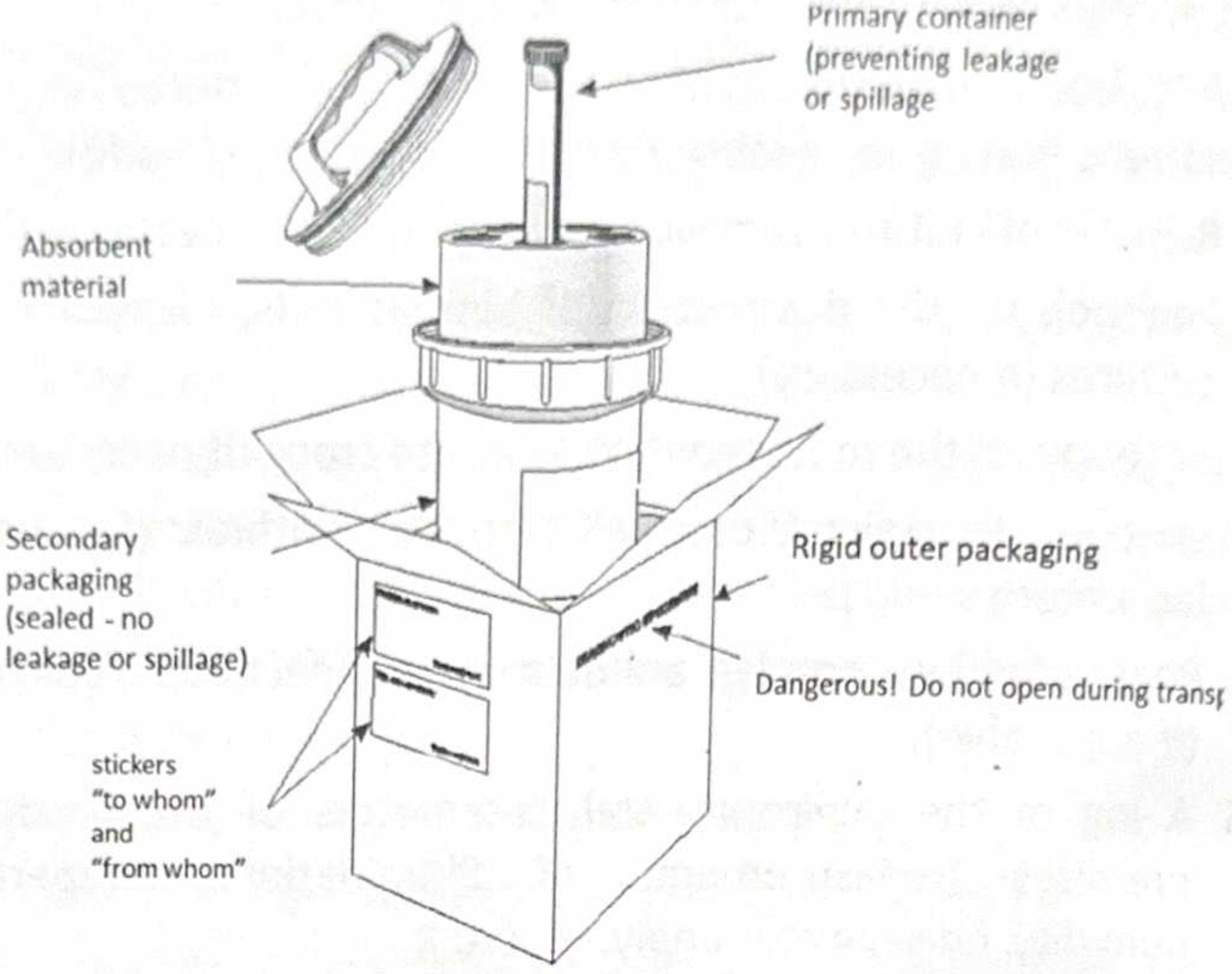


Figure 5 – Triple packingy.

1) the primary receptacle is a sealed labelled container/tube/vial;
2) secondary container – a leak-proof, durable watertight, non-leaking container filled with absorbent material; several primary containers can be placed in one secondary container;
3) the outer packaging is a sturdy thermally insulating container, with refrigeration elements if necessary.

Accompanying documents (official letter, handover/acceptance certificate, packing certificate, power of attorney, strain certificate, if applicable), including the technical data sheet, are placed between the secondary packaging and the outer packaging.

The outer packaging has a label stating the Consignor, Consignee, a sign – «Danger! Do not open during transport» and transport conditions. When unpacking the parcel, the containers, bins, and tank are treated with disinfectant solution.

An important aspect of administrative measures is the response algorithm for laboratory emergencies.

In case of an accident during work with infectious material, stop work immediately and inform the head of the laboratory (sound the alarm) and the management.

All emergencies are recorded in a special log [8, 28] and the causes of the accident are investigated and discussed.

A distinction is made between emergencies with aerosol formation, without aerosol formation, in a biosafety cabinet and with a breach of skin integrity.

In case of an accident involving splashing of pathogens and formation of aerosols (broken tubes or vials with liquid culture, splashing of bacterial suspension from a pipette or syringe, etc.) activate the emergency alarm and all persons in the room, if possible by holding their breath, immediately leave the laboratory, go to the changing room or corridor. In the changing room, carefully remove protective clothing, irrigate or soak it with disinfectant solution, and place it in a waste bag or container with disinfectant solution; treat exposed body parts with 70° ethyl alcohol, rinse mouth and throat with 70° ethyl alcohol (if necessary) and put antibiotic solutions into eyes and nose to which the pathogen is sensitive. When dealing with deep fungal pathogens, 1% boric acid is injected into the eyes and nose. In an accident with botulinum toxin, the eyes and mouth are washed with water and an antitoxic serum diluted to 10 international units in 1 millilitre. If botulinum toxin comes into contact with exposed skin, wash it off with plenty of soap and water. In case of an accident involving an unknown pathogen, prophylactic treatment with broad-spectrum antibacterials and/or antiviral agents is given.

Personnel who was involved in an accident with splashing of microbial pahtogens of pathogenicity group I are placed in an isolation ward under medical observation for the duration of the incubation period with prophylactic treatment, and a daily monitoring of body temperature. Personnel who was involved an accident with splashing of pathogens of pathogenicity group II will be subjected to medical observation and prophylactic treatment, if necessary.

In the room where the accident has occurred, personnel in a type I protective suit disinfect the accident site and all objects and switch on the bactericidal irradiators.

In an accident without splashing biological material, personnel in the room apply a swab (napkin) with disinfectant solution to the area where the biological material came into contact with the surface, treat other surfaces and nearby objects, materials, turn on bactericidal irradiators, and treat exposed body parts with 70° ethyl alcohol if necessary. Personnel leave the laboratory for the changing room and remove protective clothing immerse and put it in disinfectant solution or autoclave bag

In the event of an accident inside the biosafety cabinet, other work with infectious material is stopped immediately, a swab (napkin) with disinfectant solution is applied to the area where the biological material comes into contact with the surface of the equipment, the bactericidal irradiators are activated, the protective suit is removed and dipped into the disinfectant solution or placed in a bag (tank) for autoclaving. After exposure, the spilled material is collected and placed in a container for disposal. Exhaust ventilation remains switched on during accident and disinfection.

In an accident involving skin integrity, blood is squeezed out of the wound into a tissue dampened with a disinfectant solution; when dealing with an HIV infection, the victim is given prophylactic antiretroviral therapy (post exposure prophylaxis, PEP) within 72 hours and a follow-up is established for 3 months after the «emergency», with diagnostic tests for a HIV infection after 1 month.

Medical supervision and health screening of laboratory staff.

The medical surveillance and health screening programme includes health checks for staff on recruitment and subsequent annual check-ups. If necessary, staff should receive specific immunisations, most often for laboratory personnel working with EDI. The medical surveillance programme includes (but is not limited to) the following items: medical examinations by specialists and general practitioners; serum selection, testing and storage; immunisations; and other possible tests. Only

persons who meet specific specified medical admission requirements (e.g. immunised) may enter the laboratory unless it has been properly decontaminated in advance.

The laboratory in the «contagious» and «clean» areas must have a first-aid kit complete in accordance with the regulated requirements [29]:

1. Non-sterile bandages and/or sterile bandages.
2. Bactericidal tape and tourniquet.
3. Brilliant green and iodine or iodine wipes.
4. Citramon.
5. Corvalol.
6. Validol.
7. Alcohol or alcohol wipes.
8. Ammonia (ammonia 10%).
9. Tonometer.
10. Stethoscope.
11. Gloves.
12. An antihistamine (or epinephrine).
13. Sterile spatula for the oral area.
14. Mucus suction pump.
15. Ambu bag.

The laboratory should have an effective rodent and insect control programme, usually contracting a specialist company to carry out disinsection and deratisation.

The laboratory shall be kept clean and tidy. Junior laboratory staff shall be instructed on how to clean the laboratory areas: clean area with detergents, contagious area with the addition of disinfectants. Separate marked equipment for each area shall be used for cleaning.

Medical waste management regulations relating to administrative measures to reduce biorisk will be dealt with separately in Part 4.

In general, the administrative measures presented to reduce biorisk address the «human» factor, are not costly, do not take long to implement and are effective.

3.3 Training of staff in biosafety

Effective personnel management ensures biosafety (by employing suitable personnel) and biosecurity (by employing reliable personnel) in the laboratory [40, 44].

Personnel fitness is ensured by biomedical measures, which include a range of preventive, curative and anti-epidemic measures:

- personnel must undergo a pre-employment and a routine annual medical check-up at the time of recruitment to detect any contraindications to vaccinations, treatment with specific medication and the use of personal protective equipment;
- the head of the organisation annually approves lists of persons admitted to work with biological agents and if a new protocol, SOP, instructions is applied. The conditions for admission are a medical examination, vaccination, instruction or knowledge of biological safety (passing a test), and practical skills.

Reliability of staff is ensured by measures of background checks of laboratory staff by the human resources department:

- persons aged at least 18 years must be allowed to work;
- pregnant women, breastfeeding mothers, persons with absolute (permanent) or temporary medical contraindications, as well as staff during observation periods (before planned business trips and leaves of absence) may have restrictions on admission to work with pathogens;
- professionals with higher and secondary medical, biological or other qualifications are permitted to work in the laboratory after attending biosafety courses and learning how to work safely with pathogenic microorganisms;
- professionals with higher and secondary education, engineering and nursing staff are instructed in biosafety and biosecurity at the time of their employment;
- persons not permanently employed by the organisation shall be admitted to the laboratory by written permission of the head of the organisation after a biosafety briefing, the purpose of the visit

and its duration to be recorded in the logbook;

- visits to the laboratory by engineering staff shall be allowed when accompanied by laboratory staff and recorded in the logbook.

Laboratory personnel shall be aware of the hazards and associated risks in the laboratory as well as safe working procedures, safety precautions, emergency preparedness and response. Professionals employed shall receive annual health and safety training [31].

All staff, including non-laboratory staff, shall receive an initial induction on biosafety and biohazards at the time of recruitment. A template for the initial induction programme can be found in Annex 4. Periodic briefings on various biosafety and biosecurity issues (PPE, medical waste, working in a biosafety cabinet, cleaning and disinfection, packaging and transport of biomaterials, emergencies, etc.) are also provided to laboratory staff with documented confirmation.

Only persons trained in working with pressure vessels shall be allowed to work on the autoclave.

Laboratory staff working with pathogenicity group 1 microorganisms shall have their body temperature taken at the end of the working day and the results recorded in a log, signed by the person in charge of the thermometry.

If respiratory symptoms or other symptoms associated with occupational disease or fever occur, the laboratory staff member shall notify the head of the organisation and shall be isolated immediately until an ambulance arrives.

For laboratories dealing with highly dangerous pathogens, the reliability of personnel is of particular importance. Background checks and special training may be required before gaining access to a restricted area. Photo identification cards for staff with access to restricted areas and temporary cards for escorted visitors may be used to establish the identity of staff. These factors should be considered as part of the local risk assessment procedure when developing a biological defence plan. Procedures for approving and authorising visitors to enter controlled areas, especially access to cultures of pathogens, are required in such organisations. All staff with access to controlled areas should be trained in biological defence procedures.

In addition to instructional training, laboratory personnel with secondary and tertiary education shall receive training in the form of appropriate certification courses and continuing education.

Basic principles for laboratory work with dangerous microorganisms of pathogenicity groups 1-2 include the following requirements [2, 40]:

1. All handling of infectious material must take place inside a class 2 biosafety cabinet.
2. Respect the principle of pairing when carrying out work.
3. Compliance with Good Microbiological Practices and Procedures (GMPP/GLP).
4. Proper cleaning and decontamination of the biosafety cabinet after work is completed.
5. Taking a full shower after completing the work and getting out of the «contagious» area.

General requirements for the operation of medical laboratories to ensure the safety of the entire laboratory process are included in the training programmes and include the following:

1) a documented Biosafety Manual and SOPs should be available to all personnel;

2) all personnel including visitors, trainees and others entering and working in the laboratory shall wear carefully buttoned protective laboratory clothing;

3) long hair shall be tied back or covered so that it does not come into contact with hands, samples, containers or equipment;

4) it is forbidden to eat, drink, smoke, store any food, use cosmetics, wear jewellery, insert or remove contact lenses in the laboratory. Contact lenses may only be worn when other forms of vision correction are not applicable;

5) open wounds, cuts, scratches and abrasions must be covered with bandages of waterproof material;

6) storage of materials in the laboratory that are not intended for use or cannot be easily decontaminated (journals, books,

correspondence) should be kept to a minimum. Work with documentation, preparation of reports shall be carried out outside the area where manipulation with hazardous materials is carried out;

7) laboratory protective clothing must not be worn outside the laboratory and must not be kept in contact with personal clothing;

8) all hazardous manipulations of biological material as well as manipulations involving aerosol production (shaking, centrifugation, etc.) must be carried out in a Class 2 biological cabinet, which must be certified annually;

9) hands shall be washed after removing gloves, before leaving the laboratory and each time after handling infectious or suspected infectious material;

10) work surfaces shall be cleaned and decontaminated with disinfectant at the end of the working day as well as after each sprinkling of potentially hazardous pathogens. Work surfaces, utensils, materials and equipment that have become permeable to biological materials (cracked, chipped, etc.) must be replaced or repaired;

11) contaminated materials and equipment removed from the laboratory for maintenance, disposal or other purposes shall be properly disinfected, packaged, labelled or marked;

12) the performance of the autoclaves used for decontamination using chemical indicators shall be monitored at each load, and biological indicators should be used on a monthly basis. Test results and records of autoclaving cycles (time, temperature, pressure) should be recorded in a logbook and kept in the archive;

13) record daily the temperature regime in the refrigerators, the operating time of the UV lamps and the temperature/humidity conditions in the rooms;

14) the use of needles, syringes and other sharp objects should be kept to a minimum. Care should be taken when handling needles and syringes to avoid accidental insertion of material into oneself and the formation of aerosols during use. Needles should not be bent, cut, re-capped or disconnected from the syringe. After use, they should be placed in a sharps container resistant to puncture;

15) disinfectants active against the pathogens in use must always be available in sufficient quantities in the areas where work or storage of infectious material takes place;

16) instances of spillage of bio-material, contact with infectious material, skin tears and other incidents should be immediately reported to the laboratory manager and the biosafety officer and a record kept of the measures taken to control the epidemic;

17) staff shall wash hands with water and by dispensing liquid soap from a dispenser and hands are dried with disposable paper towels. After work, staff hands are treated with a disinfectant solution or 70° ethyl alcohol.

To ensure the effectiveness of the training process, training programmes include theoretical and practical sessions on biosafety and biosecurity. Theoretical skills are taught through lectures, presentations and held in conference rooms equipped with projectors and laptops. A training laboratory is used to practise practical biosafety laboratory skills. During practical sessions, best practice cases and simulations on emergency response, emergency evacuation from the laboratory for research staff, etc. are trained.

Pre- and post-tests are used to assess the theoretical knowledge and demonstration of practical skills in the training laboratory. In Annex 5 there are test templates for laboratory staff with higher and secondary education, untrained (nurses, disinfectors), for zoologists and parasitologists travelling in the field to epizootically hazardous areas and for engineering staff.

Biosafety and biosecurity knowledge of laboratory personnel shall be assessed annually, and in some organisations, this may take the form

of a staff competency assessment. Knowledge assessments are often conducted during an internal laboratory biosafety and biosecurity audit. Biosafety competency assessment is defined as a system for establishing and documenting the competency of personnel. The purpose of the competency assessment is to identify biosafety issues in the staff and to correct them before they affect the staff. There are the following methods of competency assessment:

- direct observation of the employee's work technique during the work process;
- the use of a checklist;
- checking records, minutes and journals completed by the employee;
- situation tasks to assess knowledge and problem-solving skills.

The results of the competence assessment are communicated to the employee and the head of laboratory. In case of non-compliance by more than 20%, a corrective action plan detailing the necessary training shall be developed. The plan shall be prepared in writing, specifying the required training and the time frame for its implementation, and describing the resources.

The appraisal is broader than the competence assessment and, in addition to biological safety issues, includes elements such as technical competence, productivity, people skills, information security, punctuality and professional conduct.

The NSCEDI has a Modular Staff Training Programme, which has 3 levels and several modules at each level (Annex 6) and is aimed at laboratory staff with higher and secondary education, at engineering technical and administrative staff.

3.4 Use of personal protective equipmenty

The use of personal protective equipment must be based on national requirements, biological risk assessment and available laboratory capacity.

Personal protective equipment (PPE) is specially designed clothing and equipment worn by laboratory personnel to protect them from infection. These include:

- ɜlaboratory coats, aprons and coveralls, armbands;
- shoes;
- gloves;
- eye and face protection;
- respiratory protection;
- head and hearing protection.

PPE is a key control measure to minimise potential hazards in procedures involving pathogens. Important factors are proper use and disposal of PPE, adequate provision of PPE in laboratories, and proper barrier properties of PPE to minimise the likelihood of infection of laboratory personnel.

A review of intralaboratory contamination cases shows that the most significant factors that have led to exposure to biological agents include inappropriate use of personal protective equipment [32, 33, 38]. Training staff in the correct use of PPE is therefore an important aspect of biosafety.

In the «clean» area of the laboratory, personnel shall wear a medical suit consisting of a top and bottom, laboratory shoes, a cap and gown if necessary. The medical suit shall be worn in the cloakroom and kept separate from personal clothing in a designated clean, dry area to prevent contamination. The following requirements for protective clothing must be met: the medical suit must have long sleeves and a fastener in the front so that the suit cannot be removed over the head; the laboratory shoes must be closed, waterproof, with non-slip soles and disinfection-resistant.

Personnel may additionally wear the following types of PPE to work in the «contagious» area if necessary: surgical type gown or overalls, cap, respirator, goggles or face shield, one or two pairs of gloves, shoe covers or separate shoes for the contagious area, apron and armbands.

PPE is used once, unless otherwise specified by the manufacturer

or agreed for multiple use. PPE must be changed if it is damaged or contaminated. Reusable PPE (e.g. safety goggles/shields) must be decontaminated after each use according to the manufacturer's instructions. PPE must be sized according to personnel clothing size. Open-toed lab shoes and short-sleeved suits without front fasteners are prohibited.

In Kazakhstan, the use of PPE in health-care organizations, including laboratories, depends on the level of protection (Table 9) [34].

Table 9 – Algorithm for the use of personal protective equipment.

Level of protection	Components of PPE
Protection 1 (minimum)	Medical cap disposable Respirator (N95 or FFP3) or disposable medical mask depending on risk Disposable non-woven dressing gown with long sleeves and latchets on the back Nitrile/latex gloves
Protection 2 (medium)	Medical cap disposable Respirator N95 or FFP2 Disposable non-woven gown with long sleeves and latchets on the back or disposable protective coveralls with a hood An apron is necessary if the dressing gown (overalls) is not resistant to liquids. Nitrile/latex gloves Safety goggles or face shield Work shoes made of waterproof material
Protection 3 (maximum)	Medical cap disposable Positive air supply filtering respirator (PAPR) or respirator type N95, FFP2, N99, FFP3 depending on risk Disposable hooded waterproof protective coveralls or disposable gown made of non-woven material with long sleeves and latchets on the back An apron is necessary if there is a risk of splashing body fluids if the gown (overalls) are not resistant to fluids. Nitrile/latex gloves Safety goggles or face shield Work shoes made of waterproof material

The use of reusable type I-IV protective suits is also regulated, depending on the work performed with microorganisms of pathogenicity groups I-IV [8]:

1) Type I – medical suit, medical cap, large headscarf (hood), anti-plague gown or overalls, positive pressure hood respirator, cotton gauze mask (or air mask or PAPR), goggles (or face shield), medical gloves (two pairs), towel, socks, closed lab shoes (waterproof boots). For hazardous work, an additional waterproof apron and sleeves and a respirator with a mechanical supply of HEPA filtered air with positive pressure – PAPR must be worn.
2. Type II – medical suit, medical cap, large headscarf (hood), anti-plague gown or overalls, cotton gauze mask (or PAPR), medical gloves (two pairs), towel, socks, closed lab shoes (waterproof boots).
3. Type III – medical suit, medical cap, large headscarf, anti-plague gown, mask or respirator, gloves, towel, socks, closed lab shoes.
4. Type IV – medical suit, cap, anti-plague gown, socks, gloves, closed lab shoes.

A reusable and a disposable set of protective clothing must be equivalent (figure 6).

Respiratory protection is classified according to air filtration efficiency (Table 10).

Table 10 – Classification of respirators in the European Union and the USAi

Filter characteristics	EU classification	Filtration efficiency (%)	Classification of the USA	Filtration efficiency (%)
Low efficiency	P1 (FFP1)	80	N95	95
Average efficiency	P2 (FFP2)	94	N99	99
Very high efficiency	P3 (FFP3)	99	N100	99,97

PPE for the «contagious» area is worn in the airlock when entering the «contagious» area and additional PPE is worn when entering the «contagious» section to work with infected animals. The first pair of gloves is worn under the sleeve of the overalls/jackets, the second pair is worn over the overalls/jackets and must be secured. In case of a scarf, a respirator or cotton gauze mask must be worn over the scarf; in case of a coverall with a fused hood, a respirator or cotton gauze mask must be worn under the hood.

When leaving the «contagious» area, the PPE must be removed into containers/bags for decontamination and subsequent disposal; contaminated PPE must be removed carefully, folding the outer side of the clothing inwards! After each piece of clothing has been removed, treat hands with antiseptic.

Gloves must be worn for all procedures that may put the hands in direct contact with biohazardous material. The first pair of gloves should be removed in the workplace, the second pair should be removed before leaving the contaminated area of the laboratory and should be decontaminated along with other waste material before disposal. At the end, hands must be washed thoroughly with soap and water and dried.

The area for donning PPE is equipped with PPE storage cabinets and a mirror. The place for removing PPE shall be equipped with a mirror, containers and/or bags of different volumes to collect PPE (for microorganisms of pathogenicity group 1-2 – class B, for microorganisms of pathogenicity group 3-4 – class B), a spray gun with skin antiseptic and wipes shall also be available.

Important: The areas for donning and doffing protective clothing must not overlap.

Sufficient provision of PPE according to international standards is also important in biosafety. According to the recommendations of the European Union Centres for Disease Control (ECDC), the calculation for 1, 5 and 25 suspected or confirmed cases of COVID-19 should meet the following standards (Table 10) [36].

Kazakhstan regulations establish requirements for the provision of disposable and reusable sets of protective suits in medical organisations, including laboratories, of different territorial levels in the field of sanitary and epidemiological well-being of the population in the following volume in case of particularly dangerous infections (Table 11) [36].

The full cycle of PPE use in the laboratory includes the following points: provision of sufficient PPE in the laboratory, selection and appropriate use of PPE, training of staff in the use of PPE, effective disinfection and subsequent disposal of PPE.

Table 11 – Number of PPE per 1, 5 and 25 suspected or confirmed COVID-19 cases

Number of PPE	A suspicious case	A confirmed case	
		Mild symptoms	Severe symptoms
Total for 1 case	3-4	11-12	12-21
A total of 5 cases	15-20	55-60	60-105
A total of 25 cases	75-100	275-300	300-525
One protective kit includes respirator (N95, FFP2 or FFP3), goggles or face shields, long-sleeved waterproof lab coat, gloves, lab shoes			

The choice of use of PPE according to international standards is not determined by a prescriptive instructional approach, but by an approach based on biological risk assessment and evidence, where the choice and use of protective clothing will be proportionate to the biorisk identified, while being appropriate to the specific laboratory environment [2, 40]. An important component of the biorisk assessment is to take into account the control measures available to mitigate these risks. It is therefore important to conduct an effective biorisk assessment when selecting PPE, taking into account the resources available.

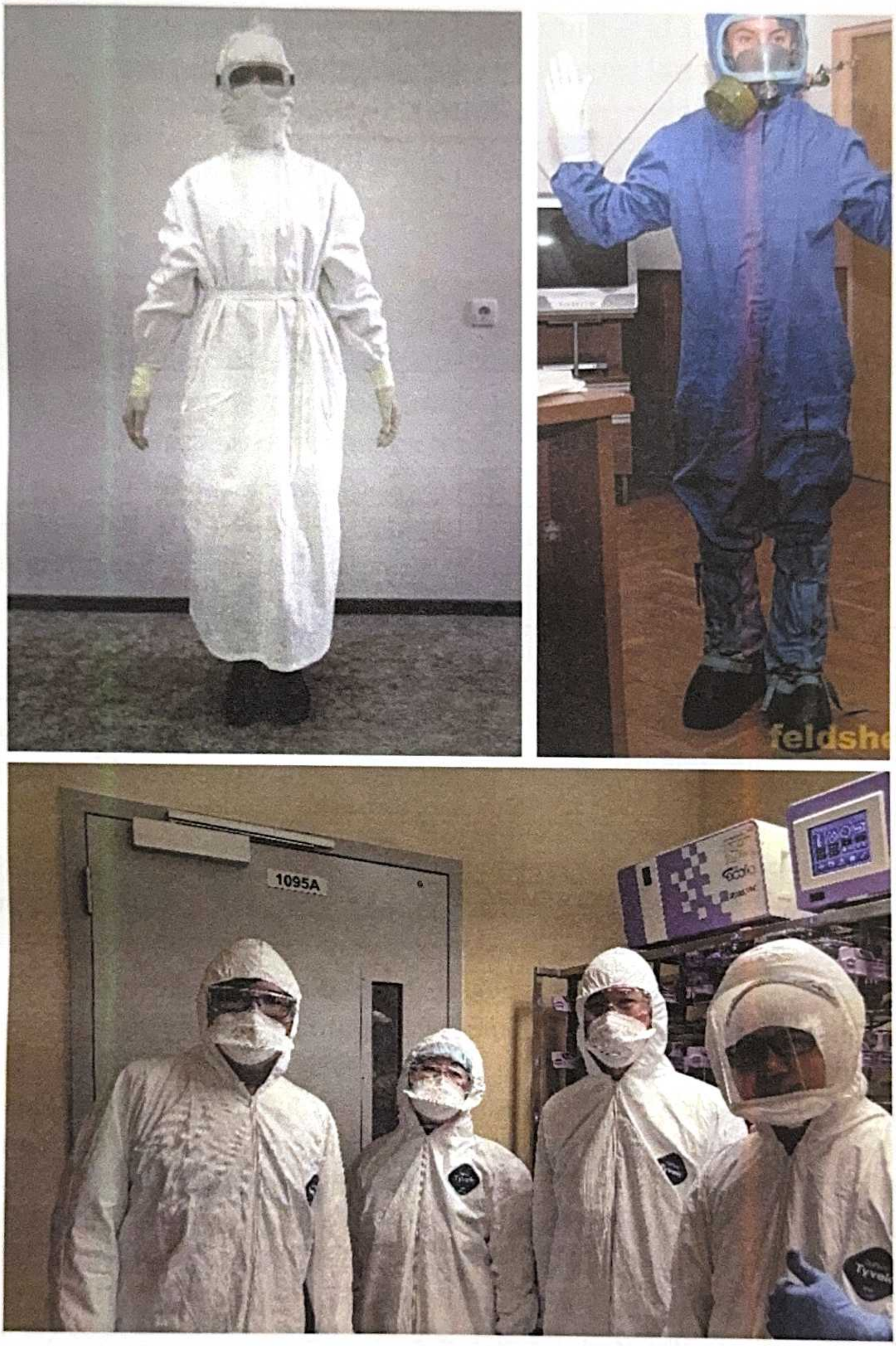


Figure 6 – Reusable and disposable protective clothing set

Table 11a – Number of sets of protective suits, personal protective equipment in health-care organisations and laboratories

№	Organisations	Set of type I reusable protective suits*, not less	A set of disposable protective clothing, at least
1	Ambulance and emergency stations	5	50
2	District and city-level infectious diseases hospitals	50	500
3	Regional-level infectious diseases hospitals	75	1000
4	District level laboratories of the National Centre of Expertise	10	40
5	Regional level laboratories for especially dangerous infections of the National Centre of Expertise	20	500

The choice of use of PPE according to international standards is not determined by a prescriptive instructional approach, but by an approach based on biological risk assessment and evidence, where the choice and use of protective clothing will be proportionate to the biorisk identified, while being appropriate to the specific laboratory environment [2, 40]. An important component of the biorisk assessment is to take into account the control measures available to mitigate these risks. It is therefore important to conduct an effective biorisk assessment when selecting PPE, taking into account the resources available.

The PPE training programme includes topics that should be periodically monitored by tests:

- The choice of use of PPE according to international standards is not determined by a prescriptive instructional approach, but by an approach based on biological risk assessment and evidence, where the choice and use of protective clothing will be proportionate to the biorisk identified, while being appropriate to the specific laboratory environment [2, 40]. An important component of the biorisk assessment is to take into account the control measures available to mitigate these risks. It is therefore important to conduct an effective biorisk assessment when selecting PPE, taking into account the resources available.
- The PPE training programme includes topics that should be periodically monitored by tests.

FIT-check – the respirator tightness check, which performed each time the respirator is donned by laboratory personnel and staff training is required.

FIT-test – testing the insulating properties.

The algorithm for the FIT-check is shown in Appendix 7.

Appropriate PPE regulations are an integral part of the Laboratory Biorisk Management Manual or the Infection Control Programme in health-care organizations (hospitals and outpatient clinics) [37].

PPE availability, selection and use of PPE are part of safety culture, and includes biorisk assessment, good microbiological practice and procedure (GMPP), training of personnel, reporting of incidents involving biological agents to reduce risks [2, 8, 15].

3.5 Internal audit of biosafety and biosecurity in the laboratory

In addition to the assessment of biorisk of laboratory procedures, an annual internal audit of biosafety and biosecurity compliance is performed in the laboratory. Internal auditing is an effective measure to control biological risk mitigation measures. The main objective of internal audits is to identify and analyse non-conformities and to make recommendations for their elimination, ans so preparing the laboratories for external audits.

The internal audit (internal evaluation) is based on the identification of non-conformities in the functional and technical condition and status of engineering, organisational and administrative measures, personnel training and personal protective equipment by checklists in the specific laboratory. Templates for checklists for all sections are provided in Annex 8.

A checklist is a method of auditing in order to identify weaknesses, deficiencies and areas for improvement. The checklist for the laboratory shall be developed and adapted depending on the purpose of the audit: self-inspection, internal audit, external audit.

The general requirements for auditing by means of checklists include the following rules:

- before the audit, a general meeting is held or an internal audit order is prepared, indicating the programme and the composition of the auditors;
- control questions should be clear, understandable, and open, such as: «show me please...», «tell me please...», you can ask leading questions;
- each test question should have a paragraph referring to a standard or legislative act;
- the interview is conducted during working hours and at the interviewee's workplace;
- the survey can start by asking you to describe your work, you can explain the reason for the survey and comment on any notes you make;
- review documents: make sure that the Biosafety Manual, Policy, SOPs and other documents are complete, up to date, and periodically reviewed;
- review records: make sure that laboratory records (personnel files, incident reports, log books, audit reports, etc.) are properly maintained and kept;
- keep track of the sample from the time it is received until the report is issued and stored;

- check the extent to which any result can be verified by staging an in-lab quality control;
- review the results of staff qualification checks, whether they have been analysed and whether corrective action has been taken;
- talk to the medical staff to get their views on the operation of the laboratory;
- the audit should be conducted in a friendly atmosphere, the interview should be conducted in a relaxed atmosphere, and the interviewees should be thanked for their participation and cooperation.

The checklists developed are optimal indicators for laboratory evaluation and can be used by the medical director, biosafety expert and any laboratory manager for auditing and identifying biosafety irregularities. These checklists can be further developed and supplemented with other important indicators, including international indicators, improving biosafety testing in the laboratory.

A simple scoring system was used to assess the results: yes, no, or unacceptable. On the basis of this assessment, the proportions of compliance for each section and the need for certain measures were determined:

- below 50% – significant improvements are needed in the laboratory, limiting hazardous work and correcting non-compliances immediately;
- indicator between 50% and 85% – some improvement is needed;
- indicator is above 85% – the laboratory is in a good situation.

When non-conformities are identified, it is recommended that the first focus is on correcting observations relating to organisational and administrative decisions as well as those relating to PPE and staff training. These non-conformities do not incur significant financial costs and can be implemented immediately or within the next few months. In the WHO Laboratory Biosafety Manual, it is noted that the use of appropriate working practices and techniques by trained staff in appropriate protective clothing is the primary protective measure against laborato-

ry inhalation contamination and that «no safety box or other device or technique will in itself guarantee safety unless users employ safe working practices based on awareness and understanding» [2, 15].

Non-conformities relating to planning and biosafety engineering measures are costly and can be implemented over a long period of time without affecting the safety of personnel. In the long term, engineering non-conformities need to be addressed, as by international standards they are among the most effective measures and do not depend on 'human factors'. For example, for Kazakhstan laboratories working with microorganisms of pathogenicity groups 1-2, it is primarily recommended to improve the supply and exhaust air ventilation system with air filtration through fine filters, the procedure for personnel access to the laboratory in the form of an electronic key, and the installation of door closers on all doors of the contagious area.

Various audit programmes are available, e.g. WHO Laboratory Quality Assessment Tool, 2012. [5, 41, 46]. The company Integrated Quality Laboratory Services (www. igls.net) developed a laboratory safety audit system in 2017 which contains indicators in 9 sections:

1. Premises and work flows.
2. Training and personnel management.
3. Laboratory methods and practices.
4. Cleaning, decontamination, sterilisation and management of medical waste.
5. Emergency situations.
6. Biorisk management.
7. Documentation and regulations.
8. Biosecurity.
9. Other risks.

The internal audit report includes a cover sheet, sections (general characteristics of the hazardous facility, indicators of the degree of emergency risk, characteristics of accidents and injuries in the organisation, characteristics of the organisational and technical measures ensuring the safety of the facility and emergency preparedness). The last sheet contains signatures of the developers.

The internal audit report shall be attached:

1) 1) a situational plan showing the consequences of possible emergencies at the site, with only the most dangerous and most likely scenarios for emergencies given;

2) calculations on facility risk indicators, indicating the methods of risk assessment;

3) materials substantiating and confirming the risk level of the facility to the personnel and the public living nearby;

4) probability and degree of risk of emergencies (natural and man-made);

5) recommendations for the development of measures to eliminate or reduce biological risks to the maximum permissible level.

Based on the non-conformity analysis, an action plan is approved to eliminate or reduce biological risks to the maximum permissible level. When implementing the action plan, a person responsible for monitoring the effective implementation of the action plan shall be appointed.

Important: After a certain period of time, the auditor visits the laboratory again to check that the discrepancies have been corrected.

Internal auditing is the monitoring of laboratory biosafety and biosecurity activities by an auditor to assess the biosafety status of the laboratory. The checklist determines whether the laboratory is performing properly and reliably, whether the laboratory is well managed and has good laboratory practices, and which areas of the laboratory need improvement.

PART IV.
MEDICAL WASTE MANAGEMENT

The laboratory must have an approved Medical Waste Management Program, where the main principles are [2, 8, 9, 10, 42, 43]:

1) 1) minimization of biological risks in the handling, collection, transportation, processing and disposal of waste;
2) minimizing the harmful effects of medical waste on the environment and minimizing the generation of hazardous medical waste..

The purpose of the Medical Waste Management Program is to develop and approve procedures for the management and disposal of medical waste, generated in the laboratory, to reduce waste generation and ensure the proper collection, identification, sorting, packaging, decontamination, storage, transportation and final disposal of waste. These procedures protect personnel, the environment and the public from potential contamination and/or exposure to hazardous materials and are a prophylactic against laboratory-acquired infections.

Field of application:

- this Program is applicable to all laboratory personnel, including professionals, nursing staff, technical and service personnel, students / trainees, invited specialists, involved in «X» activities;
- personnel directly involved in the handling of medical waste should receive qualified documented training on the safe collection and disposal of medical waste. The training is conducted by the responsible person for medical waste by order of the director of the NSCEDI once a year (the training program is presented below).

The composition of generated waste by class

The main risk factor for infection, associated with medical waste, is unprotected contact with contaminated bags and containers for medical waste and accidental injections with contaminated needles.

Attention! All manipulations with medical waste must be carried out in protective clothing and PPE: gown or pyjamas/jumpsuits, gloves, masks/respirators, lab shoes, apron and armbands (if necessary).

The laboratory employee, creating the waste, is responsible for the correct collection, sorting, treatment and transport of the waste.

Disposable/reusable containers and disposable bags for medical waste and also laboratory containers with appropriate disinfectant solution must be available in each workplace. If necessary, a common waste collection area may be set up in each laboratory room.

All medical waste is differentiated by hazard class:

- class A, non-hazardous waste – waste that does not come into contact with the biological fluids of patients, with infectious patients, non-toxic waste, food waste from all departments of medical organizations, except infectious (including dermatovenerological) and phthisiatric departments, furniture, equipment, faulty diagnostic equipment that does not contain toxic elements, construction waste, non-contaminated paper, etc.;
- class B, hazardous waste – infected and potentially infectious waste (materials and tools, things contaminated with blood and/or other biological fluids), pathological waste, organic operational waste (organs, tissues), waste from infectious diseases departments (including food), waste of microbiological laboratories working with microorganisms of pathogenicity groups III-IV, biological waste from vivariums;
- class C, extremely hazardous waste – materials that have been in contact with patients with infectious diseases that can lead to emergencies in the field of sanitary and epidemiological welfare of the population, waste from laboratories working with microorganisms of pathogenicity groups I-II, waste from

mycological, TB hospitals, waste from patients with anaerobic infection;

- class D toxicological waste – expired medicines, waste from medicinal and diagnostic preparations, disinfectants that are not to be used, expired, cytostatics and other chemical preparations, mercury-containing appliances, instruments and equipment, waste of raw materials and products of pharmaceutical industries, waste from the operation of equipment , transport, lighting systems;
- class E, radioactive waste – all types of waste, in any state of aggregation, in which the content of radionuclides exceeds the permissible levels established by radiation safety standards.

Medical waste, depending on the class, is collected in sacks/packs and containers that have the appropriate color:

- class A, non-hazardous waste – black;
- class B, hazardous waste – yellow;
- class C, extremely hazardous waste – red;
- class D, toxicological waste – white;
- class E, radioactive waste – labelled «radiation hazard».

Each bag and container for medical waste must have the following information «Medical Waste. Class «X»» with the name of the unit, date; name and surname of the person responsible for collecting the waste.

All solid and liquid waste must be collected at the end of each working day in appropriate bags and containers for subsequent decontamination, transportation, storage and disposal.

Solid waste includes cotton and gauze materials, used gloves, nutrient media bottles, plastic utensils, tips, paper packaging, etc. Liquid waste includes liquid chemicals and pharmaceuticals, used liquid nutrient media, solutions, disinfectants, sterilants, etc.

Separately distinguish biological medical waste – waste associated with experimental animals and material from humans: animal carcasses; materials contaminated with biological fluids and products

of laboratory animals; postoperative and sectional remains; biological samples (including blood, serum, plasma, urine tubes; syringes after injections or blood collection); feed residues; bedding. Biological waste is collected separately from other waste.

The bags and/or containers are maximum filled to ¾ capacity and sealed with tape, then handed over to the temporary medical waste room to the person in charge of waste collection, filling in the form in the logbook.

Do not crush medical waste with your hands or collect or disassemble medical waste without personal protective equipment.

Moisture proof containers are used for collecting liquid organic medical waste, with a lid to ensure they are sealed.

Flammable chemical waste, corrosive chemical waste and oxidising chemical waste must not be mixed with each other in any combination. Information on the chemical can be found on the relevant Material Safety Data Sheets (MSDS).

If the type of waste is one of the following, it is considered hazardous and must be segregated from other waste:

1. *Toxic:* a substance that can cause death, bodily injury or harm to a person if swallowed, inhaled or in contact with the skin.
2. *Explosive:* a substance which is usually unstable, explosive, reacts violently with water, produces toxic gases, vapours or smoke when reacting with water, or contains cyanides or sulphides which are capable of producing toxic gases, vapours or smoke.
3. *Combustible:* substance having a flash point below 60°C
4. *Corrosive:* substance having a pH less than 2.0 or greater than 12.5.

Compatible chemicals available in small quantities may be collected in appropriately labelled containers and stored temporarily in fume cupboards and disposed of when the specified volume is reached.

If there is mixed waste, such as chemicals and infectious material, the chemical material should be neutralised first and only then the infectious material should be decontaminated.

The hard-walled moisture-resistant container can be reused for the placement of infectious and non-infectious waste if:

- each time it is emptied, it is thoroughly rinsed and decontaminated;
- container surfaces are fully protected against dangerous contamination by a single-use, non-piercing and undamaged cladding material or a bag to be disposed of together with infectious waste;
- the surface of the trim material is not damaged or pierced.

Waste management procedure: the waste management cycle consists of the following stages: determination of the class of medical waste (A, B, C, D, E), collection and disinfection of medical waste, packaging and labelling of medical waste, transportation and storage of medical waste, disposal of medical waste.

Algorithm for collecting, transportation and storing class A medical waste:

1. Class A waste is collected in black disposable bags or reusable containers. Waste containers are labelled «Medical waste. Class A». Waste is disposed of in general containers for solid household waste (SHW). Containers for the collection of solid waste are equipped with lids.
2. Class A waste is transported to a household waste site: this is a special site, fenced on three sides to a height of 1.5 m, equipped with a canopy to protect against precipitation, should be paved and be convenient for vehicle access and loading and unloading operations.
3. Class A medical waste is removed every three days.

Algorithm for collecting, transportation and storing class B and C medical waste:

1. Class B and C medical waste are collected in single-use bags and single-use or reusable solid (not punctureable) yellow or red containers, which shall be labelled «Medical Waste. Class B or C» with the name of the unit, date, name and surname of the person responsible for waste collection.

2. The bags or containers are maximum filled to ¾ capacity and sealed with tape, then handed over to the temporary medical waste room to the person in charge of waste collection, filling in the logbook according to the form.

3. Do not crush medical waste with your hands or collect or disassemble medical waste without personal protective equipment.

4. Class B liquid organic medical waste is collected in moisture-resistant containers with a lid to keep it sealed.

5. Class B and C wastes are subject to mandatory decontamination at the place of their generation, that is, in the laboratory, with subsequent disposal.

6. Class B and C liquid waste must be decontaminated (disinfected) and then discharged into the sewage system.

7. Class B and C pathological and organic surgical medical waste (organs, tissues, etc.) must be cremated (incinerated) or buried in cemeteries in a designated area without prior decontamination.

8. When organising waste disposal using an incinerator, class B medical waste can be collected and stored without pre-decontamination.

9. Export of non-decontaminated class B medical waste outside the structural unit and the territory of the organization is not allowed.

10. When decontaminating medical waste by autoclaving, it must be collected in yellow or red autoclavable bags, respectively.

11. Transportation reusable containers must be watertight and fitted with tightly closing lids. Reusable containers should be disinfected and washed after emptying the medical waste content.

12. Every day, decontaminated, packaged and labeled waste bags/ containers are collected in a laboratory at a specific location and then transported in an appropriate form to a temporary medical waste storage facility.

13. Transportation of packaged medical waste from laboratories to the temporary waste storage facility is carried out daily on a special trolley or directly by the responsible laboratory personnel.

14. Acceptance / transfer of medical waste for temporary storage is carried out in a properly packed form (tightly closed, without punctures and leakage of liquid), with qualitative and quantitative records in a special journal (Tables 12 and 13), which indicate the date, name of the unit, class and amount of medical waste, name of the handed over and accepted employee.

15. The final disposal of medical waste of class B and C is carried out by thermal action (burning) on medical waste at a temperature not lower than 1000 – 1200°C. Utilization is carried out by a specialized company, licensed for this type of activity, under a contract.

16. For temporary storage of medical waste of class B and C a separate equipped room is provided at the facility with equipped supply and exhaust ventilation, refrigeration and freezing equipment for storing medical waste, racks, containers for collecting packages with medical waste from departments, a sink with hot and cold water, UV lamp, spray bottle with antiseptic.

Algorithm for collecting, transportation and storing class D medical waste:

1. Class «D» medical waste shall be collected in labelled containers and/or white bags labelled «Medical Waste. Class D», indicating name of unit, date, name of person responsible for waste collection.

2. Used fluorescent lamps, mercury-containing appliances and equipment are collected in tightly sealed containers to prevent breakage during transport and are transferred to a temporary storage room for centralised disposal under contract with a specialised organisation.

3. Non-toxic solid chemical waste is collected in a garbage container for centralized disposal of solid waste.

4. Non-toxic liquid chemical waste is discharged into the sewer system.

5. Toxic chemical waste that can be neutralised is neutralised and discharged to the sewer system, followed by flushing with running water.

6. Liquid chemical waste that cannot be neutralised is collected by group in polyethylene canisters of up to 10 litres with a screw cap, filled to a maximum of 90% and deposited in a temporary storage room. All canisters are labelled with the date of packing, name and waste group. The collection of such waste is carried out centrally by contract.

7. Pharmaceuticals, medicines and medical devices may be disposed of in their original packaging or in cardboard boxes. The boxes are labelled with the date of packing, name and waste group. Pharmaceuticals, medicines and medical devices in glass containers should not be disposed of as biological waste. The contents should be poured into cardboard boxes.

8. Rules for neutralisation of chemical waste. Waste from strong mineral acids (sulphuric acid, spent oleum solutions,

chloro- and fluorosulphonic acid solutions in sulphuric acid, chloric acid, nitric acid, hydrochloric acid) as well as water and alcoholic alkaline solutions must be neutralised before discharge into the sewer system. These wastes are corrosive and, for the most part, toxic and can cause severe chemical burns. Therefore, they must be neutralised in a fume cupboard that is in good working order and in compliance with the safety regulations for handling corrosive substances. Before starting work, wear protective equipment (gown, acid-resistant gloves, goggles or face shields, preferably an apron and sleeves made of rubberised fabric).

9. Acidic and alkaline wastes should be neutralised. Concentrated solutions must be pre-diluted with water so that the concentration of acid (alkali) in the resulting solution does not exceed 10%. Dilution is carried out in an open container such as a porcelain beaker. It should be kept in mind that large quantities of heat may be generated during this operation. Therefore, the diluted liquid is carefully added to the calculated amount of cold water or crushed ice in small portions while stirring.

10. When neutralising acidic solutions, an aqueous solution of technical sodium hydroxide with a concentration of no more than 10% is added in small portions while stirring, and when neutralising alkaline solutions, a solution of diluted hydrochloric acid (concentrated acid is first diluted with 2.5 volumes of water).

11. The neutralisation is monitored with suitable indicator strips. A solution with a pH value of 7 is considered neutralised. If this value cannot be achieved, the neutralisation is continued as described above, dividing the neutralised solution into 2-3 parts. The neutralised solutions are discharged into the sewage system.

12. Class D medical waste is disposed in hazardous waste landfills or, if neutralised, in the SHW landfills.

Algorithm for collecting and storing class E medical waste:

1. Class F radioactive medical waste is managed in accordance with the national regulations.
2. Radioactive material must be collected in designated containers before it is ready for disposal.

Waste treatment (decontamination) and disposal methods:

1. All laboratory wastes generated in «contagious» areas should be considered as potentially infectious medical wastes, which are class B or C and require decontamination at the point of generation.
2. Decontamination is carried out by autoclaving, chemical treatment or other alternative methods.
3. The mode of autoclaving and chemical disinfection of the medical waste shall be determined by the head of the unit in accordance with the risk assessment.
4. All waste collection containers and bags must be treated with chemical disinfectants on all sides before being transported or before being removed from the biosafety cabinet or chemical fume hood.

Table 12 – Log book for registration of the medical waste acceptance / delivery

_____ for 20____

(name of the healthcare facility)

Date	Depart-ment	Medical waste class	Number	Name who delivered	Name who accepted

Table 13 – Logbook for daily registration of medical waste.

_____ for 20____

(name of the healthcare facility)

Date	Class A (m3)		Class B								
			Biological / anatomical waste (kg)			Sharp, stabbing waste (kg)			Others (kg)		
	Collected	Transferred for decontamination (disposal)	Collected	Transferred for decontamination (disposal		Collected	Decontaminated	Transferred for decontamination (disposal)	Collected	Transferred for decontamination (disposal)	

Table 13 – *Table continuation*

Class C								
Biological / anatomical waste (kg)			Sharp, stabbing waste (kg)			Others (kg)		
Collected	Decontaminated (disposal)	Transferred for decontamination (disposal)	Collected	Decontaminated (disposal)	Transferred for decontamination (disposal)	Collected	Decontaminated (disposal)	Transferred for decontamination (disposal)

Handling regulations with sharp and stabbing medical waste:

1. Sharp and stabbing objects include broken glass, syringe needles, opened ampoules, feathers/shavers, surgical instruments, pipette tips, needles, scarifiers, scalpels. Of these, scalpels and knives must be decontaminated and reused.
2. Sharp and piercing objects are collected in special sturdy, non-piercing and watertight containers with an airtight lid (sometimes with a needle-opener), bearing a biosafety label, name of the unit, date, name of the person responsible for waste collection:
    a. class B waste is yellow;
    b. class C waste is red.
3. Used stabbing and other sharp objects are placed in a container without prior dismantling, rinsing, disinfecting immediately after use.
4. Place the container in a suitable place for use and fill no more than ¾, close tightly and place in a suitable bag. Never fill the container completely.
5. The container in the bag should only be moved carefully closed and handed over to the temporary medical waste room to the person in charge of waste collection, with the form completed in the logbook.
6. The container in the bag must be disposed of without prior dismantling.
7. Never transfer the contents of the sharp's disposal container to another container.
8. Never remove the lid on the sharp's container.
9. If there are special devices for needle separation (needle pickers, needle destructors, needle cutters), used syringes without needles are collected in disposable soft (bags) with other medical waste to be decontaminated and then disposed of.

Training of staff in waste management rules:

Laboratory personnel should periodically receive documented instructions or training on approved rules for the management of

medical waste.

In summary, the proper handling of medical waste from laboratories includes the following general requirements:

1) disposable, waterproof bags and reusable containers with tight-fitting lids are used for waste collection;
2) bags and containers should have different colours (waste class A – black, B – yellow, C – red, D – white) and appropriate labelling (medical waste class, laboratory name, responsible person and date) for each waste class;
3) stabbing objects, including needles, scalpels, metal and glass objects, are placed in closed waterproof containers with a special hole in the lid. Syringes are introduced into these containers immediately after use indiscriminately;
4) appropriate bags and containers for medical waste should be available at every workplace and should be no more than ¾ full. Before taking out of the workplace, the filled bag is closed and wiped with a napkin moistened with a disinfectant solution;
5) decontamination of medical waste is carried out by autoclaving and / or immersion in a disinfectant solution or another alternative method is used;
6) for temporary storage of medical waste of class B, C, D, a separate equipped room is provided at the facility (equipped with supply and exhaust ventilation, refrigeration equipment for storing biological waste, racks, containers for collecting packages with medical waste from departments, a sink with hot and cold water supply, UV lamp);
7) filled containers should be removed daily from the work area and stored before decontamination or final disposal in a specially designed place;
8) persons, who carrying out the transportation of medical waste from the moment of loading onto a vehicle until they are accepted at the designated place, must comply with the measures for the safe handling of them.

APPENDICES

Annex 1

BIORISK ASSESSMENT REPORT *(form)*

Name of SOP / Project _____

Responsible performer of the procedure: _____

Laboratory and available biorisk mitigation measures: _____

_____

The result of the biorisk assessment: _____

_____

Description of biological (hazardous) materials	
Pathogen, pathogenicity group:	
Procedure and the most dangerous manipulations (divided into procedural steps)	
Purpose:	

Procedure step	Description of activities	Threat (what can go wrong)	Consequences (code)	Probability (code)	Level of initial biorisk, taking into account available control measures	Additional control measures (if necessary)	The level of final biorisk
1.							
2.							
3.							

Performers of the procedure: _____

full name, position, length of work, education/training

PPE used: _____

Date: _____

Signature of the person who performed the biorisk assessment _____

(if applicable)

Protocol of the meeting of the Biosafety Committee _____

(if applicable)

Annex 2

PATHOGEN BIOHAZARD SPECIFICATION FORM

Created by (full name, position) _____

Date of creation _____

Revised by (full name, position) _____

Reason for revision _____

Date of revision _____

_____

I. General information about the pathogen

Phylum (optional): _____

Family: _____

Genus: _____

Species: _____

Other *(serotype, biovar, etc.)*: _____

Morphological characteristics: _____

Spore formation: _____

Intracellular localisation: _____

II. Threats to health

Pathogenicity group: _____

Causes a disease: _____

Human pathogen: _____

Pathogen of terrestrial animals: _____

Pathogen of aquatic animals: _____

Pathogen of bees: _____

Causes the laboratory acquired infections: _____

Causes a disease, that to be registered: _____

Causes a disease for which the notification is issued: _____

Causes a disease for which an immediate notification is issued:

Causes a deadly disease: _____

Causes a disease in animals from the WOAH list: _____

Primary threats: _____

Biological materials as a source of contamination: _____

Special threats: _____

Incubation period: _____

Main symptoms _____

III. Биоқауіпсіздік

Policy of isolation: _____

Pathogenicity: _____

Is it an aerosolising pathogen: _____

Infectious dose: _____

Is it a zoonotic pathogen: _____

Host: _____

Vectors: _____

Transmission: _____

Contagiousness: _____

Personal protective equipment: _____

Vaccination: _____

Specialprecautions: _____

Storage: _____

Disposal: _____

IV. Sustainability

Sensitivity to antibiotics: _____

Resistant to antibiotics: _____

Sensitivity to disinfectants: _____

Physical inactivati on: _____

Survival outside the host organism: _____

V. Incidents

Actions in the event of a spill: _____

Prevention after exposure: _____

Preventive treatment: _____

VI. Severity of the consequences:

Disastrous consequences _____

Severe consequences _____

Moderate consequences _____

Insignificant consequences _____

Annex 3

JOB INSTRUCTIONS FOR BIOLOGICAL SAFETY OFFICER

Responsibilities:

1) supervises the compliance of laboratory personnel with biosafety rules and requirements;
2) organises the collection and study of scientific and technical information on biosafety issues;
3) conducts audits of laboratory facilities to assess existing biological risks and develop measures to address them, including annual internal audits and assessments of staff biosafety competence;
4) participates in the investigation of accidents involving biological materials and the implementation of remedial measures, organises the notification of responsible persons in accordance with the applicable SOPs, and provides accident records;
5) assesses biological risks before carrying out dangerous procedures;
6) conducts all types of biosafety training for staff (list of briefings and trainings if necessary).

Biosafety officer is obliged to:

1) participate in the preparation of the laboratory work plan and biosafety internal audit report for the current year;
2) participate in the organisation and delivery of initial and refresher training on biosafety and biosecurity, including administrative, technical and security staff;
3) review documents (reports, programmes, etc.)
4) participate in the development of methodological, training and regulatory documents;
5) participate in the preparation of requisitions for equipment, reagents and consumables, including PPE, autoclave control indicators, disinfectants, medical waste bags;
6) monitor the management of medical waste in the laboratory.

Rights::

The biosafety officer has the right to::
1) demand that management provide the necessary conditions for the performance of their duties;
2) seek advice from experts in biosafety and biosecurity;
3) report any shortcomings identified in the course of the activity and

make proposals for remedying them;
4) improve their qualifications through seminars or courses..

Responsibility:
The biosafety officer is personally responsible for:
1) the proper performance of his or her duties as set out in these instructions;
2) the quality and timeliness of the performance of its tasks;
3) the security of documents in execution;
4) observance of performance discipline.

Qualification:
1) basic training in: Public health, Public health care, Preventive medicine, Hygiene-epidemiology;
2) at least 3-5 years' laboratory experience;
3) training at certification courses on biosafety and biosecurity under the program of the standard curriculum of the Republic of Kazakhstan on biosafety.

Instructions read: _____ _____

signature *full name*

Annex 4

«APPROVED»:
Director of the Science Centre

_____
full name

«____» _____ 20____

INITIAL BRIEFING PROGRAMME ON BIOSAFETY AND BIOSECURITY

(draft)

1. Rules for staying on the territory of the laboratory and in laboratory rooms.
2. Briefly the concept of biosafety and biosecurity.
3. A brief introduction to the laboratory biological risks.
4. Layout of the laboratory (briefly on zoning and admittance). Rules for entry-exit to the laboratory, escorting unauthorised persons into the laboratory.
5. No food or water intake, no smoking, no chewing gum in the laboratory. Hand treatment.
6. Rules for storage, wearing and disposal (decontamination) of PPE in the laboratory.
7. General rules for working with complex equipment.
8. Notification in case of temporary incapacity for work or in case of symptoms of diseases similar in clinic to OIH.
9. Potential hazards of disinfectants, flammable and corrosive substances. Storage regulations.
10. The need to notify the Superintendent of all laboratory emergencies.
11. The concept of laboratory emergencies. Spill response (if necessary).
12. Regulations for the disposal of medical waste in the laboratory. Medical waste management programme (if applicable).
13. Rules for dealing with infected animals (if necessary).

Annex 5

TEST ASSIGNMENT:
«Biosafety and biosecurity issues for laboratory professionals»
TEST

1. **What can lead to the formation of aerosols?**
   A) opening vials/ampoules with lyophilised cultures
   B) titration of serological material with a pipette on an open table
   C) shattering of labware with liquid infectious material
   D) all of the above

2. **The main steps of medical waste management include:**
   A) collection, disinfection, labelling, storage, disposal
   B) labelling, storage, disinfection, collection, disposal
   C) collection, labelling, storage, cremation
   D) disinfection, collection, labelling and disposal

3. **Biosecurity is:**
   A) protection of flora and fauna
   B) care for the environment and natural resources
   C) protection of pathogens (germs) from unauthorised use
   D) protection of humans from contamination

4. **If there is a «Biological Spill/Accident» sign hanging on the door of the laboratory to which you have been summoned:**
   A) have to go in wearing a medical mask
   B) you can enter in a type 1 protective suit
   C) have to enter wearing a Tyvek coverall
   D) you can enter holding your breath to clarify the situation

5. **Biosecurity is:**
   A) protection of flora and fauna
   B) care for the environment and natural resources
   C) protection of pathogens (germs) from unauthorised use
   D) protection of humans from contamination

6. **Class C medical waste is collected in bags or containers in:**
   A) white colour
   B) black colour
   C) red colour
   D) orange colour

7. **When removing the disposable respirator, it is very important not to touch:**
   A) its outer surface
   B) its inner surface
   C) the respirator rubber bands
   D) the valves on some respirators

8. **Who is responsible for carrying out the biological risk assessment of the procedure and/or project?**
   A) biosafety specialist
   B) head of laboratory, principal researcher, biosafety specialist
   C) no one, once the assignment/contract is received, you can start work
   D) chairperson of the Biosafety Commission

9. **Which of the following practices is used when working in a biosafety cabinet?**
   A) disinfection of the BSC working surface before and after work
   B) disinfection of all items brought in and out of the BSC
   C) prohibiting the storage of anything in the BSC
   D) all of the above

10. **How is biological material transported from a laboratory to another facility?**
   A) carry the material in a special bag, accompanied by documents
   B) carry the material in an unbreakable container, accompanied by documents
   C) carry the vial with the material in a sealed container and outer transport box/bag
   D) all of the above

TEST ASSIGNMENT:
«Biosafety and biosecurity issues for zoologists and parasitologists»»
TEST

1. **What are the most common and dangerous routes of contact between humans and microorganisms?**
   A) contact with skin or mucous membranes
   B) ingestion
   C) inhalation
   D) through damaged skin - cuts, punctures, lab animal bites

2. **The main steps in the management of medical waste in the field include:**
   A) collection, disinfection, labelling, storage, cremation
   B) labelling, storage, disinfection, collection, disposal in a pit
   B) collection, disinfection, labelling, storage, disposal in a pit
   D) disinfection, collection, storage and cremation

3. **Biosecurity is:**
   A) protection of flora and fauna
   B) care for the environment and natural resources
   C) protection of pathogens (germs) from unauthorised use
   D) protection of humans from contamination

4. **Respirator is:**
   A) a mask made of special filtering material to protect the upper respiratory tract from inhaling contaminated air
   B) standard medical mask
   C) standard medical mask made of cotton fabric
   D) all of the above

5. **Biosafety is:**
   A) protection of flora and fauna
   B) care for the environment and natural resources
   C) protection of pathogens (germs) from unauthorised use
   D) protection of humans from contamination

6. **Class B and C medical waste is collected in bags or containers in:**
   A) white colour
   B) black colour
   C) red and yellow colours
   D) orange colour

7. **When removing the disposable respirator, it is very important not to touch:**
   A) its outer surface
   B) its inner surface
   C) the respirator rubber bands
   D) the valves on some respirators

8. **Who is responsible for carrying out the biological risk assessment of the procedure and/or project?**
   A) biosafety specialist
   B) head of laboratory / principal researcher
   C) no one, once the money is received, you can start work
   D) chairperson of the Biosafety Commission

9. **Disinfection of catching tools includes (choose correct answers)?**
   A) treatment with disinfectants
   B) firing treatment
   C) treatment by insolation during the warm season
   D) all of the above

10. **How is biological / field material transported to the laboratory?**
   A) under triple-package conditions
   B) in an unbreakable container, accompanied by documents
   C) cotton or calico bag containing the corpse of the rodent in a sealed container/bag and outer transport box/bag
   D) all of the above

TEST ASSIGNMENT:
«Biosafety and biosecurity issues for engineering staff»
TEST

1. **Before repairing any equipment that bears the «Biohazard» sign, you must:**
   A) self-treat it with sodium hypochlorite
   B) treat it with 70% alcohol by yourself
   C) check with the laboratory manager that the equipment is decontaminated
   D) make an application for gas decontamination of the equipment.

2. **When working together with a contracting engineer, he or she should be accompanied:**
   A) everywhere in the laboratory
   B) only when working in BSL-3 laboratories
   C) only when working in hazardous areas
   D) only if he/she asks you to do so

3. **Biosecurity is:**
   A) protection of flora and fauna
   B) care for the environment and natural resources
   C) protection of pathogens (germs) from unauthorised use
   D) protection of humans from contamination

4. **If there is a «Biological Spill/Accident» sign hanging on the door of the laboratory to which you have been summoned:**
   A) have to go in wearing a medical mask
   B) you can enter in a type 1 protective suit
   C) have to enter wearing a Tyvek coverall
   D) you can enter holding your breath to clarify the situation

5. **If you spill a tank of concentrated acid on yourself while carrying it in the corridor, you should**
   A) urgently contact a medical doctor at the NSCEDI
   B) immediately inform the biosafety officer
   C) call for emergency
   D) use an emergency shower

6. Biological waste bags usually in:

A) white colour
B) black colour
C) red-orange colour
D) blue colour

7. When removing the disposable respirator, it is very important not to touch:

A) its outer surface
B) its inner surface
C) the respirator rubber bands
D) the valves on some respirators

8. What is the first thing to do if a chemical solution gets into an employee's eyes?

A) run to the nearest sink and wash your eyes
B) inform the biosafety officer
C) put a solution of hydrogen peroxide in your eyes
D) contact a medical doctor at the NSCEDI

9. If you hear a fire alarm:

A) proceed to the evacuation assembly point without using the lift
B) do not leave the building until directed to do so by the director or chief engineer
C) check the cause with the engineer on duty
D) stand in safe places marked with an umbrella

10. The fact that the material from the autoclave is really disinfected can be found out:

A) by asking a member of the laboratory staff
B) by the colour of the chemical indicator
C) by the special deformation of the waste bags
D) by bag surface temperature

TEST ASSIGNMENT:

"Biosafety and biosecurity issues for laboratory technicians "
TEST

1. What can lead to the formation of aerosols?

A) opening vials/ampoules with lyophilised cultures
B) titration of serological material with a pipette on an open table
C) disposal of labware with liquid infectious material
D) all of the above

2. The main steps of medical waste management include:

A) collection, disinfection, labelling, storage, disposal
B) labelling, storage, disinfection, collection, disposal
C) collection, labelling, storage, cremation
D) disinfection, collection, labelling and disposal

3. What can disrupt air circulation in a biosafety cabinet (BSC)?

A) walking people in front of the BSC
B) placing objects on the front grille or cluttering the rear grilles
C) opening and closing the doors of the laboratory
D) all of the above

4. The following types of PPE must be worn when accepting and processing samples from humans for investigation of microorganisms from pathogenicity groups 1-2:

A) medical suit, overalls with hood, medical mask, shoe covers/lab shoes, 2 pairs of gloves and goggles
B) medical suit, overalls with hood, respirator, shoe covers/lab shoes, gloves and face shield
C) medical suit, plague-proof gown, boots or shoe covers, respirator, gloves, goggles
D) medical suit, disposable gown, cap, shoe covers, 2 pairs of gloves and goggles or face shield

5. Biosafety is:

A) protection of flora and fauna
B) care for the environment and natural resources
C) protection of pathogens (germs) from unauthorised use
D) protection of humans from contamination

6. Class B medical waste is collected in bags or containers in:

A) white colour
B) black colour
C) red colour
D) yellow colour

7. When removing the disposable respirator, it is very important not to touch:

A) its outer surface
B) its inner surface
C) the respirator rubber bands
D) the valves on some respirators

8. Can put on a cap on the syringe/needle only with gloves?

A) Correct
B) Wrong

9. Which of the following practices is used when working in a biosafety cabinet?

A) disinfection of the BSC working surface before and after work
B) disinfection of all items brought in and out of the BSC
B) prohibiting the storage of anything in the BSC
D) all of the above

10. How is biological material transported from the laboratory to another facility?

A) carry the material in a special bag, accompanied by documents
B) carry the material in an unbreakable container, accompanied by documents
C) carry the vial with the material in a sealed container and outer transport box/bag
D) all of the above

TEST ASSIGNMENT:
«Biosafety and biosecurity issues for disinfectors»

TEST

1. **1. What are the most common and dangerous routes of contact between humans and germs in the laboratory?**
   A) contact with skin or mucous membranes
   B) ingestion
   C) inhalation
   D) through damaged skin - cuts, punctures, lab animal bites

2. **The fact that the material from the autoclave is really disinfected can be found out:**
   A) by asking the lab technician
   B) by the colour of the chemical indicator
   C) by the special deformation of the waste bags
   D) by bag surface temperature

3. **What is PPE:**
   A) personal protective equipment
   B) public protective equipment
   C) possible protection equipment
   D) all of the above

4. **Decontamination of laboratory utensils is carried out as follows (select the correct answers):**
   A) autoclaving
   B) washing with detergents
   C) immersion in a disinfectant solution for a certain period of time
   D) all of the above

5. **The following types of protective clothing are worn when laboratory animals are infected with the plague pathogen (select the correct answers):**
   A) medical suit, plague-prone gown, medical mask, shoe covers/lab shoes, 2 pairs of gloves, headscarf and goggles
   B) medical suit, overalls with hood, respirator, shoe covers/lab shoes, gloves and face shield
   C) medical suit, plague-proof gown, boots or shoe covers, respirator, gloves, goggles
   D) medical suit, disposable gown, cap, shoe covers, 2 pairs of gloves and goggles or face shield

6. **Medical waste bags are in:**
   A) white colour
   B) black colour
   C) red and yellow colour
   D) blue colour

7. **When removing the disposable respirator, it is very important not to touch:**
   A) its outer surface
   B) its inner surface
   C) the respirator rubber bands
   D) the valves on some respirators

8. **Respirator is:**
   A) a mask made of special filtering material to protect the upper respiratory tract from inhaling contaminated air
   B) standard medical mask
   C) standard medical mask made of cotton fabric
   D) all of the above

9. **Cleaning of laboratory rooms in the «contagious» area includes (select correct answers)?**
   A) washing the floors and wiping all surfaces with a detergent solution
   B) washing the floors and wiping all surfaces with a disinfectant solution
   C) UV exposure for 30 minutes
   D) ventilate the room for 30 minutes

10. **Control of the operation of UV lamps and refrigerators includes?**
   A) daily checks of the operation of UV lamps and refrigerators
   B) daily recording of the operating hours of the UV lamps
   C) daily recording of refrigerator temperatures
   D) all of the above

Modular Biosafety and Biosecurity Training Program at the NSCEDI

Category / Levels	Specialists with higher and secondary education	Responsible person	Time frame for training	Disinfectors, engineers, security guards	Responsible person	Timeframe	Visitors, cleaning service, contractors	Timeframe for training
I – Instruction	I-1 Primary	Head of Laboratory	When hiring	I-2 Primary	Head of Labo-ratory	for training When hiring	I-3 Primary	When visiting the laboratory
G - General course	G-1 Retraining for medical doctors on EDI	ITC*	current year					
	G-2 Retraining for zoologists on EDI	ITC*	current year					
	G-3 Retraining for veterinarians on EDI	ITC*	current year					
Competence assessment	Annually on selected biosafety issues							
R – Refresh training	Biosafety/biosecurity fundamentals and BSL-2	BBO**	by order of the director	Biosafety/biosecurity fundamentals and BSL-2	BBO**	by order of the director		
	BSL-3	BBO**	by order of the director	PPE	BBO**	by order of the director		
	ABSL-3	BBO**	by order of the director	Medical waste	BBO**	by order of the director		
	Advanced course on biosafety and biosecurity	BBO**	by order of the director	FIT- check	BBO**	by order of the director		
	Basic biosafety for engineers	BBO**	by order of the director	Biosecurity for security guards	BBO**	by order of the director		
	Medical waste management	BBO**	by order of the director					
	FIT-check / test	BBO**	by order of the director					
P – personnel certification	By order of the director	By order of the director						

*ITC - International Training Centre, **BBO - Biosafety and Biosecurity Office

Annex 7

FIT-CHECK PROCEDURE FOR N95 /N99 / FFP2 / FFP3

The FIT-check is a check to ensure that the respirator fits snugly over the face.

This procedure must be carried out each time the respirator is put on in front of a mirror and includes the following steps:

1. Turn the straps of the respirator outward so that it does not interfere when putting on.
2. Place the respirator on the palm of your hand and then place it firmly against your face.
3. First place the upper strap on the back of the head with the other free hand, then the lower strap on the back of the neck.
4. Make sure that the straps are not crossed over.
5. Make sure that the respirator fits comfortably over your face.
6. Place the fingers of both hands on the bridge of the nose and press the nasal clip to fit the respirator tightly over the nose.
7. You must use the fingers of both hands when pressing the nose clip. If you do this with one hand, there is a risk of a loose fit of the respirator.
8. The next important step is to check the fit – this is the FIT-check:
   - wrap both hands around the respirator and take a few intense breaths in and out through your mouth;
   - if you notice air leaking around the edges of the respirator while breathing in and out, adjust the face mask, straps and nose clip to ensure that the respirator mask fits snugly over the face;
   - repeat the inhalation and exhalation procedure again. Make sure that the respirator fits snugly so that there is no air leakage during the inhalation and exhalation.
9. Procedure for removing the respirator:
   - do not touch the outer surface of the respirator with your hands;
   - first gently remove the lower strap from the neck;
   - then carefully remove the strap from the back of the head;
   - avoid sudden movements and shaking;
   - carefully place the used respirator in a class B / C waste sack / container;
   - wash your hands thoroughly with liquid soap and dry them.

Annex 8

CHECKLISTS FOR INTERNAL AUDIT ON BIOSAFETY AND BIOSECURITY AT THE LABORATORY

1 SECTION
Planning, engineering measures and equipment to ensure biosafety and biosecurity

Full name of interviewer _____

Full names of all interviewee persons _____

Indicators	Yes	No	N/a
The laboratory is separated from public areas by a door (point 7, order 105).			
Laboratory doors provide restricted access by means of an access control system (point 13, order 105).			
The name of the laboratory and the "Biohazard" sign shall be marked on the front door (point 16, order 105).			
Zoning of the laboratory into dirty and clean areas (poit 67, annex 1, table 2, order 105).			
Whether the layout of the premises excludes the crossing of clean and contagious streams (point 17, annex 1, table 2, order 105).			
Availability of a sanitary locker (cloakroom) for the entrance to the 'clean' area (point 8, order 105), where personal and laboratory clothing are stored separately.			
Availability of a sanitary pass for entry to the 'contagious' area (sanitary pass) (point 82, order 105).			
Required laboratory space by type of work (annex 1, table 2, order 105).			
Availability of a regulated set of rooms in the infectious disease unit (annex 1, table 2, order 105).			
Two exits (separate for staff and separate for samples) (point 9, order 105).			
Existence of an emergency exit.			
Each entrance and exit is marked with an emergency exit sign.			

Doors of sanitary facilities have door closers (point 106, order 105).			
Doors to the cubicle and pre-box have visible windows (point 16, order 105).			
The presence of signs on laboratory doors indicating their purpose (point 16, order 105).			
Grilles on all ground floor windows of the laboratory (point 12, order 105).			
Mosquito nets for windows to protect against insects (point 16, order 105).			
Doors, frames, furniture, table surfaces must be non-absorbent (i.e. organic materials must be avoided in their construction) (point 25, order 105).			
Internal surfaces in laboratory rooms (floors, walls, ceilings) are smooth, without crevices, easy to clean, resistant to detergents and disinfectants, no slippery floors are allowed (point 20, order 105).			
Floors (sealed, non-slippery, resistant to corrosive liquids) (point 20, order 105).			
Skirting boards (sealed, built-in) (point 22, order 105).			
The room where infected animals are handled has thresholds 30 cm high (point 85, order 105).			
Luminaires of the "closed" type.			
Availability of hand washing sinks, mirrors and containers with disinfectant solutions in the laboratory (point 29, order 105).			
Availability of visual aids on proper handwashing.			
Heating appliances are smooth, accessible for cleaning from all sides, to be washed and disinfected daily.			
Availability of a cold water supply (point 27, order 105).			
Availability of hot water supply (point 27, order 105).			
Availability of a supply and exhaust ventilation system (point 34, order 105) with artificial stimulation and separate (self-contained) ventilation devices for air extraction from fume cupboards.			

The rooms of the "contagious" area of the laboratory shall be equipped with a supply and exhaust ventilation system with artificial inducement and fine filters at the outlet. For district level laboratories, mechanical forced ventilation is permitted. (point 222, order 105).			
The direction of air flow inwards is always ensured in such a way that it goes into the infected zone, i.e. into the negative pressure zone (this creates a pressure difference of 12 to 35 Pa) .			
Availability of artificial and natural lighting (point 33, order 105).			
Alarms (point 124, order 105).			
Sanitary facilities, toilets, pre-boxes shall be equipped with hand wash basins with liquid soap (point 89, order 96).			
Washbasins are equipped with electric towels or disposable towels (point 89, order 96).			
State of physical protection of the laboratory – fencing, perimeter lighting and access procedures (points 9, 10, 13, order 105).			
A walk-through autoclave (point 89, order 105) for handling Group I bacterial pathogens and Group I-II pathogenicity viruses in the contagious area of the laboratory.			
The autoclave is marked as a pressure vessel (point 77, order 105).			
Availability of Class 2 Biosafety Cabinets (BSCs) in bacteriological cubicles (point 18, order 105).			
Existence of BBB certification (point 79, order 105).			
Availability of serviceable UV equipment in the "contagious" area (points 19, 68, 92, 94, order 105).			
Availability of necessary laboratory equipment – refrigerators, thermostats, centrifuges, pipettes, microscopes, etc.			
Total non-conformities detected:			
Total non-conformities detected in %:			

2 SECTION

Management and administrative activities to ensure the biosafety in the laboratory

Full name of interviewer _____

Full names of all interviewee persons _____

Indicators	Yes	No	N/a
Current authorisation to work with microorganisms of pathogenicity groups 1-4 (point 41, order 105).			
Availability of nomenclature, laboratory regulations, job descriptions.			
Authorisation order for personnel to work with pathogenicity group 1-2 microorganisms.			
Presence of a biosafety specialist (point 5, order 758).			
Contingency and emergency response plans, including a developed warning system, a plan for dealing with deliberate (threat of removal, removal, theft) or unintentional (accidental release, fire, earthquake) situations.			
Availability of health and safety instructions (point 43, order 105).			
Availability of a logbook on biosafety and biosecurity training.			
Availability of a register of staff safety briefings (point 43, order 105).			
Availability of a programme for the prevention of nosocomial infections (NCDs), which includes registration of NCDs and training of staff (point 160, order 96).			
Availability of an emergency logbook (point 160, order 96).			
Availability of a medical waste management programme in the laboratory/organisation (point 177, order 96).			
Order on responsible persons in charge of controlling the disposal of medical waste (point 177, order 96).			
An anthrax examination log of the premises and equipment upon completion of anthrax investigations (point 84, order 105).			
Availability of SOPs for all types of laboratory procedures performed and biosafety.			

Compliance with the rules of the register (numbered, serially numbered and stamped).			
Availability of an isolator in an organisation handling pathogens of pathogenicity group 1.			
Availability of space for temporary storage of class B and C medical waste (point 69, order 331).			
Adequate facilities for temporary storage of class B and C waste (points 80-84, order 331).			
Proper storage of class D medical waste (point 96, order 331).			
Availability of a register for the registration, recording, collection and reception of class B, C and D medical waste (point 195, order 96 and point 79, order 331).			
Availability of a contract for the disposal of class B, C and D medical waste (point 191, order 96).			
Adequate provision of a class A medical waste disposal site (points 55, 56, order 331).			
Undertake an annual medical examination (Order 131 of 15 October 2020) .			
The laboratory periodically performs documented internal audits assessing biosafety requirements - provide results of internal audits.			
Laboratory work, disinfection and cleaning.			
Changing appropriate protective clothing when entering/ exiting a "contagious" area (points 46, 57, 63, 91, order 105).			
All work related to the reception and primary processing of biological material and its examination for the detection of microorganisms of pathogenicity groups I-II shall be carried out in the contagious area of the laboratory using a type I-II protective suit (point 85, order 105).			
Procedures involving the formation of aerosols (e.g.: infestation of animals, suspension of ectoparasites, centrifugation and titration of uncontaminated material, etc.) are performed in a type I protective suit or in a BSC.			
Serum tests for detection of antigen or antibodies to pathogenicity groups I-II micro-organisms, including centrifugation, are carried out in a separate serological box or in a BSC (points 89, 103, order 105).			
Infestation and autopsy of laboratory animals and the housing of infected animals is carried out in a special contagious laboratory unit at the BSC (point 81, order 105).			

Keeping reagents separate from infected material and microbial strains.			
Labelling of all reagents and containers with disinfectant solutions.			
Presence of inscriptions on test tubes, cups, bottles with the name of the material, analysis number, dates of sowing and registration number (points 71, 193, order 105).			
Availability of containers and bags and ties for medical waste (points 177, 191, order 96).			
Proper labelling of medical waste containers and bags (points 178, 180, order 96).			
Hand washing is done by dispensing liquid soap from a dispenser and drying hands with single towels (point 54, order 105).			
Availability and staffing of an emergency first aid kit in the "contagious" area of the laboratory in case of an 'emergency' (points 54, 225, order 105).			
Availability of an emergency protective clothing set.			
Maintain cleanliness and order in the laboratory (point 68, order 105).			
Monthly cleaning schedule (point 54, order 96).			
Availability of labelled cleaning equipment in the "clean" area (point 68, order 105).			
Availability of labelled cleaning equipment in the "contagious" area (point 68, order 105).			
Sanitary rooms shall be equipped with structures for drying cleaning equipment (point 53, order 96).			
Availability of a logbook for monitoring the operation of the autoclave using chemical tests (point 79, order 105).			
Availability of an autoclave monitoring logbook using a bacteriological test.			
Availability of a UV lamp operating time logbook.			
The expiry date of the indicators is appropriate.			
Presence of skin antiseptic on workbenches (point 85, order 105).			
Bacteriological and serological cubicles have mats soaked in disinfectant solution by the doors (point 85, order 105).			
Availability of instructions and state registration certificates for available disinfectant solutions (point 52, decree 96).			
Availability of consumables (nutrients, diagnostic preparations, protective clothing and disinfectants).			

Provision of laboratory utensils.			
Keeping keys to the laboratory (keys to be handed in to the duty officer of the organisation against receipt).			
Locks and seals on thermostats, refrigerators, cabinets, doors of workrooms with pathogenicity group 2 micro-organisms (point 84, order 105).			
Accounting for the isolation, storage, transfer and destruction of microorganisms.			
Availability of authorisation for the storage of museum strains of pathogenicity group 2 micro-organisms (point 190, order 105).			
Availability of a list of available pathogenicity groups 1-2 micro-organisms with inventory numbers and responsible personnel responsible for storage of micro-organisms (point 191, order 105).			
Existence of a thermostat or crop/material flow logbook.			
Recording/recording of all incoming/existing specimens, including cultures, subcultures and other sources (infected tissue/samples or animals).			
Availability of certificates of reception, transfer and destruction of strains (points 192, 197, 198, order 105).			
Separate and store pathogens separately by pathogenicity group in signed receptacles (points 196, 193, order 105).			
Storage of pathogens in metal containers in locked and sealed refrigerators or safes (point 196, order 105).			
Availability of an inventory list in each refrigerator, safe with stored micro-organisms (point 196, order 105).			
Compliance with packaging and transport of micro-organisms and infectious material (points 200-208, order 105).			
Availability of SOPs on packaging and labelling of infectious material and package opening.			
Total discrepancies detected:			
Total discrepancies detected in %:			

*БҚШ – биологиялық қауіпсіздік шкафы.

3 SECTION

Protective clothing and personal protective equipment

Full name of interviewer _____

Full names of all interviewee persons _____

Indicators	Yes	No	N/a
Provision of the laboratory with PPE for use under normal and emergency working conditions (Annex 2, order 116*).			
Compliance with the appropriate requirements for protective clothing type 1-4 (points 56-66, order 105).			
A clear description of the choice and use of PPE in the Standard Operating Procedures (SOP) (point 56, order 105).			
Properly donning appropriate protective clothing (points 56-66, order 105) - must demonstrate.			
PPE is stored separately from personal clothing.			
Separate areas for donning and doffing PPE are available in the contagious area.			
Material contaminated or likely to be contaminated with microorganisms of pathogenicity groups I – II, dissection and contamination of animals, ectoparasites, centrifugation shall be taken in a type I protective suit (point 84, order 105) or in a disposable protective suit (overalls or pyjamas with gown, lab shoes, cap, gloves, respirator N95/FFP2, glasses or face shield).			
Staff have received documented training on how to properly put on and take off PPE.			

Personnel trained in documented instruction on how to properly wear N95/FFP2 и N99/FFP3 respirators – FIT-test.			
Availability of Type I protective clothing (or disposable protective clothing) packs for material pick-up or emergency situations.			
Having an emergency first aid kit in the "contagious" area.			
Proper decontamination of PPE (availability of and compliance with standard decontamination procedures) (points 63-64, order 105).			
Availability of containers and bags for collection of used PPE.			
Change intervals for reusable protective clothing (once or twice a week and/or as soiled) (point 217, order 96).			
Total discrepancies detected:			
Total discrepancies detected in %:			

** Қайта пайдалануға болатын қорғаныс костюмінің 10 жиынтығы және бір рет қолданылатын киімнің.*

4 SECTION
TRAINING OF STAFF TO DEAL WITH DANGEROUS INFECTIONS

Full name of interviewer _____

Full names of all interviewee persons _____

Indicators	Yes	No	N/a
Staff of the laboratory (complete set).			
Availability of an employee information folder.			
Availability of documented biosafety instruction.			
Availability of a logbook of visits to the laboratory by unauthorised persons (visitors, engineering staff, etc.).			
The availability of a daily thermometer logbook (point 84, order 105).			
Availability of documentation on medical examinations of employees with harmful and hazardous working conditions (order, contract and place of examination, lists, final certificates).			
Completion of an initial specialisation/retraining course on EDI for medical doctors and laboratory technicians.			
Trainings and advanced trainings (refresh courses, trainings, seminars, etc.) for specialists during the last 5 years.			
Completion of a documented instruction on medical waste management.			
Completion of a documented BSC instruction*.			
Documents on vaccination of professionals against plague (order, list, location, coverage, contraindications).			

Authorisation of the autoclave (point 78, order 105).			
Specialists involved in work with disinfectants (dis-instructor, disinfector, deratisator) shall undergo professional training in disinfection, disinsection and deratisation every five years (point 5, order 68 of 29.07.2022).			
Specialists involved in work with disinfectants (dis-instructor, disinfector, deratisator) are instructed annually in safe work practices and first aid in case of poisoning by disinfectants.			
Familiarising staff with the SOPs			
Total discrepancies detected:			
Total discrepancies detected in %:			

ANSWERS TO THE PRACTICAL EXERCISES

Practical exercise in section 2.2:

When dealing with pathogens of pathogenicity group 1-2, i.e. highly dangerous pathogens, it is of course necessary to complete a PSDS. Arguments: Pathogenic biological agents of pathogenicity groups 1-2 cause diseases with severe consequences, easily spread from infected to healthy organisms, for which effective means and methods of treatment and prevention, including vaccines, are available.

Practical exercise 1 in section 2.3:

When dealing with a pathogen of pathogenicity group 1 but attenuated (attenuated) strain, an PSDS must be completed. Arguments: The pathogen is safe in healthy individuals with normal immunity, but the researcher may have health conditions that could lead to the development of disease in them. In addition, certain storage and cultivation conditions may alter the properties of the pathogen, including virulence.

Practical exercise 2 in section 2.3:

Biological hazard specification of the pathogenic biological agent Yersinia pestis.

I. **General information about the biological agent**

Name: Yersinia pestis.

Type: Bacteria.

Morphological characteristic: gram-negative, ovoid, bipolar staining (Romanowsky-Giemsa).

Spore formation: none.

Intracellular localisation: facultative intracellular parasite.

II. **Threats to health**

Risk group: pathogenicity group I.

Causes a disease: plague in rodents; plague in humans with bubonic, pneumonic and septicemic forms.

Laboratory acquired infections: yes, including fatal infections.

Causes a reportable disease: yes.

Causes a notifiable disease: yes.

Causes a disease for which an immediate notification is given: yes.

Fatal disease: yes.

Causes a disease in animals from the list of WOAH: none.

Primary hazards: direct contact with the culture; direct contact with infected biological material from humans or rodents; generation of droplets and aerosols from handling the culture or contaminated biological material, accidental autoinoculation; ingestion of food in the laboratory.

Biological materials – source of infection: bubonic discharge.

Special hazards: bite of infected fleas collected from rodents.

Incubation period: 1 to 6 days; in vaccinated persons this may be prolonged by 2 days.

Key symptoms: fever, chills, weakness, headache. Bubonic form: Local lymphadenitis with significant enlargement of the lymph node (buboes). Pneumonic: rapidly progressive pneumonia with shortness of breath, chest pain, productive cough with watery, purulent or bloody sputum; within 2-4 days respiratory failure progresses and shock develops. Septicaemic form: bacteraemia, septic shock, coagulation disorders; within 2-4 days there is multiple organ failure; buboes may not be present.

III. Biosafety

Isolation policy: BSL-3 / ABSL-3 practices and equipment for all work involving crops, biological materials and rodent necropsy.

Pathogenicity: In natural conditions bubonic plague occurs following bite of infected fleas, 50% mortality in untreated; pneumonic plague can develop both primary (via aerosol infection) and secondary (when the pathogen enters the lungs through the bloodstream), 100% mortality if untreated; septicemic plague occurs in 20% of bubonic plague patients, 100% mortality if untreated.

Is an aerosolising pathogen: yes.

Infection dose: 100-20,000 germ cells.

Is a zoonotic pathogen: yes.

Reservoir: wild rodents, rabbits; raptors can also be a source of human infection. Susceptible to plague in humans and over 200 mammal species.

Vectors: fleas of wild rodents, especially rat fleas (Xenopsylla cheopis);

rarely human fleas (Pulex irritans).

Transmission: in the laboratory environment: handling infected tissues or body fluids, inhalation of droplets or bacterial aerosol, handling laboratory cultures.

Contact	Infection
Skin contact (injection, bite, scratch)	Yes
Contact with mucous membranes by splashing or contaminated hands (eyes, nose, mouth)	Yes
Inhalation	Yes
Swallowing	Unlikely

Infectivity: fleas can remain infectious for several months; bubonic plague is usually not transmitted directly from person to person; pneumonic plague can be easily transmitted from person to person under the right climatic conditions (overpopulation facilitates transmission).

Personal protective equipment: gloves should be worn when handling field or infected laboratory rodents and when direct skin contact with infectious materials is likely; a gown with tight cuffs and back ties should be worn when handling cultures and specimens; a respirator should be worn when there is a risk of contact with bacterial aerosol.

Vaccination: yes (persons working with cultures in the laboratory). The vaccine does not protect against disease by inhalation of bacterial aerosol.

Special precautions: only carry out rodent dissection in a biological safety cabinet. Treat rodents with insecticides before necropsy.

Storage: in appropriately labelled sealed containers.

Disposal: prior to disposal, decontamination with wet steam (121°C for at least 15 minutes), incineration (rodent carcasses).

IV. Sustainability

Sensitivity to antibacterial drugs: streptomycin, tetracycline, chloramphenicol (for treatment of plague meningitis), kanamycin (for treatment of children under one year of age).

Resistance to antibiotics: not generally characteristic; multidrug resistance is encoded by the plasmid.

Sensitivity to disinfectants: the pathogen is sensitive to many disinfec-

tants: 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, iodine preparations, phenols, formaldehyde.

Physical inactivation: sterilisation with moist heat (120°C for at least 15 minutes), dry heat (160-170°C for at least 1 hour).

Survival outside the host: blood – 100 days, carcasses – up to 270 days.

V. **Incidents:**

Actions in case of spills: notification of the biosafety officer, rapid response team and isolation ward doctor; isolation of the victim and close contacts for a maximum incubation period plus one day.

Post-exposure prophylaxis: monitoring of clinical symptoms with daily thermometry; administration of ELISA in casualties; initiation of prophylactic treatment no later than 8 – 24 hours from the time of the incident.

Preventive treatment: chemoprophylaxis with tetracyclines or sulphonamides in the victim and close contact persons.

VI. **Category of the severity of consequences:** severe.

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