



The Evolving Landscape of Biosafety and Biosecurity: A Review of International Guidelines and Best Practices

Mishal Safdar¹, Muneeb Ullah², Ayisha bibi², Muhammad Amir Khan³, Maha Rehman⁴, Zainab Fatima¹, Maheer Hussain¹, Uzma Azeem Awan¹, Muhammad Naeem^{1*}

¹Department of Biological Sciences, National University of Medical Sciences (NUMS), Rawalpindi, Punjab, Pakistan

²Department of Pharmacy, Kohat University of Science and Technology, Kohat, Khyber Pakhtunkhwa, Pakistan

³Department of Foreign Medical education, Fergana Medical institute of Public Health, 2A Yangi Turon street, Fergana 150100, Uzbekistan.

⁴Department of Biotechnology and Genetic Engineering, Kohat University of Science and Technology, Kohat, Khyber Pakhtunkhwa, Pakistan.



Received date: 16-10-2023

Publication date: 13-12-2023

Abstract

Biosafety and biosecurity encompass the intersection of bioengineering and biotechnology, along with the evaluation and control of risks to human, animal health, and the environment. This link encompasses the danger created by research and its use, as well as research and application to reduce risk via bioengineering and biotechnology. High-level biosafety laboratories provide a secure and reliable setting, integrating robust containment measures, well-educated staff, and precise biosafety protocols to safeguard scientists from infections while working with microbial pathogens. Simultaneously, they prevent the accidental release of these pathogens into the surrounding environment. In recent decades, there has been the construction and operation of labs with different tiers of protection, the establishment of legal regulations and a laboratory biosafety management system, and these functional labs have played a crucial role in addressing newly emerging and recurring infectious diseases. This review article offers useful insights into the complicated environment of biosafety and biosecurity at both the national and international levels. It advocates for more international cooperation among states, organizations, and stakeholders to ensure the effective implementation of biosafety and biosecurity measures, fostering a safer and more secure global biotechnology landscape.

Keywords Biosafety, Biosecurity, National framework, international guidelines, Biological Weapons Convention (BWC), International Health Regulations (IHR), World Health Organization (WHO), National biosafety regulations

1. Introduction

Biosafety involves principles, techniques, and protocols designed to prevent accidental exposure to diseases and toxic substances, as well as to avoid their unintentional release into the environment. It is not solely an labresponsibility but a collective effort aimed at safeguarding a clean and secure environment (1). The term "biosecurity" can be quite intricate as its meaning

can vary in different contexts. According to the guidelines set by the World Health Organization (WHO) (2), biosecurity involves the processes that establish and uphold security and control over dangerous microorganisms, toxins, and related materials. Laboratory biosecurity, conversely, centers on safeguarding, regulating, and responsibly managing crucial biological materials within a laboratory to prevent unauthorized access, loss, theft, misuse, diversion, or

Corresponding author at: Muhammad Naeem
Email address: m.naeem@numspak.edu.pk

<https://doi.org/10.56600/jwmdc.v2i2.73>



accidental release. While biosafety aims to shield individuals from potentially perilous pathogens, biomolecules, or chemicals, biosecurity concentrates on safeguarding these materials from individuals (3). Biosecurity principles are distinct from biosafety concepts. While the strategies employed to achieve these objectives may often overlap or complement each other, there can be situations where they are at odds (4). Global concerns about new and transboundary infectious zoonotic illnesses have raised demand for disease diagnostics, particularly in the veterinary sector. Biosafety and biosecurity are unlikely to be high-priority challenges in poor or recently established countries, as the sector frequently works with minimal resources. Various international standards and guidelines, including World Health Organization (WHO) items (5, 6), licensing or accreditation programs are accessible for evaluating and certifying institutional technological competencies and quality management in the field of laboratory research and development (R&D) involving infectious pathogens (7). These terms are often used to refer to various quality standards, including Good Laboratory Practice (GLP), International Organization for Standardization (ISO) certifications, Clinical and Laboratory Standards Institute (CLSI) criteria, and Organization for Economic Co-operation and Development (OECD) GLP principles (8).

2. National Frameworks and Guidelines

Many developing countries have utilized developed-country principles as a starting point and then modified or amended them to conform to local legislation and situations. At the international level, United Nations Industrial Development Organization (UNIDO), Food and Agriculture Organization (FAO), World Health Organization (WHO), United Nations Environment Program (UNEP), and other organizations have developed guidelines that have assisted poor nations in building their own biosafety guidelines (9). In Pakistan, a national biosafety strategy to control all biotechnology development in the country is urgently needed to address the problems (10). Enacting this strategy has the potential to enhance biotechnology research and development in Pakistan and facilitate cooperative relationships amongst native and international researchers and analytical facilities interested in collaborative research, experimentation, or on-site evaluations involving GMOs.

The main goal is to underline the creation of the following Biosafety Guidelines. The framework, developed by the National Biosafety Committee (NBC), are not designed to impose strict mandate that impede pursuits related to the advancement of recombinant DNA technology within the country (11). However, it's important to strike a balance, avoiding excessive permissiveness that might inadvertently encourage negligence and irresponsible behavior among certain researchers or laboratories (12). These guidelines cover a broad spectrum of activities involving gene manipulation through recombinant DNA technology, without regard to their specific goals. This encompasses tasks like creating biotechnologically modified plants, animals, and microorganisms, producing vaccines, manufacturing Genetically Modified Organisms (GMOs) for industrial purposes and their resulting products, and introducing GMOs into the setting for pilot studies and mercantile usages (13). The National Biosafety Committee acknowledges that these regulations are not exhaustive and anticipates that further modifications and revisions will be necessary in the future (14). As new information becomes accessible, it will be incorporated to enhance the current criteria, making them more pragmatic and supportive of the country's broader biotechnology advancement (15).

2.1 Basis of Biosafety Guidelines

The biosafety regulations aim to safeguard human health and the environment by minimizing the potential harm that could arise from laboratory activities involving recombinant DNA and the intentional venting of resulting Genetically Modified Organisms (GMOs) and their derived yields (16). Under these guidelines, the term "regulated material" comprises of all genetically altered things/ essentialities, including DNA and RNA medicinal, viroid's, viruses, cells, and other beings that have been genetically altered or manipulated. It also includes their derivatives and any waste or by-products resulting from genetic engineering procedures, whether or not they contain viable organisms (17). These Guidelines are organized into two sections. The first section addresses the handling of regulated activities in laboratories and outdoor settings. The second section outlines the approval processes necessary to declassify controlled materials, enabling their unrestricted distribution and commercial utilization.

All regulated works are divided into three groups (18) based on the amount of due hazard and refuge:

Work with little risk, B) Work with low risk, and C) Work with a high degree of danger.

Three stages of monitoring and implementation are envisaged in the proposed guidelines. First and foremost, the Principal empiricist and experiment or are accountable to themselves and the community (19). The Institutional Biosafety Committee (IBC) will oversee monitoring and inspection. The IBC is a key organ that plays a pivotal role in the overall setup. It serves as the foundation for the entire setup (20). The Committee will accept submissions, make recommendations for laboratory setup and scheduled releases, and adequately get them surveilled. All facts and findings that must be sent to the following two layers must go through the IBC, which must therefore be comprised of persons who are skilled to comprehend the potential dangers linked with each, and assess their respective significance. (21). Secondly, a Technical Advisory Committee (TAC) will be responsible for the technical review of all licensing applications, ensuring that GMOs or any related products being considered have undergone a comprehensive risk assessment in accordance with these established criteria (22). Third, the Ministry of Environment will establish a National Biosafety Committee (NBC) to serve as the overseeing authority responsible for thorough oversight, control of hazards, and the market introduction of all governed products. (11).

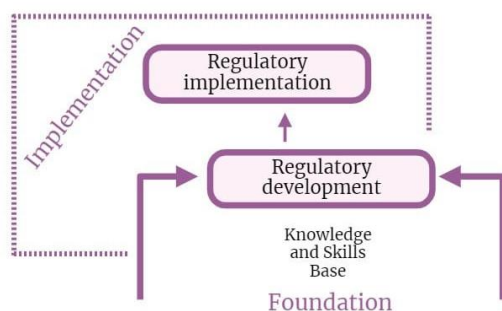


Figure 1: Basic elements providing for implementation of biosafety regulations

2.2 Scope of Guidelines

2.2.1 Laboratory Work

These rules apply to all investigative endeavors, regardless of where they take place, be it in educational

or research facilities, developmental organizations, or private enterprises, that are related to the utilization and application of GMOs and their derivatives. To ascertain whether a particular project falls within the purview of these regulations, one should prepare a proposal and submit it to the Institutional Biosafety Committee (IBC) (23). In cases where there is no adequately established Institutional Biosafety Committee (IBC) or if one is unavailable, the identical proposal should be presented to the Technical Advisory Committee (TAC) for assessment through the supervising ministry (24). Researchers who possess any doubts or questions regarding these issues are advised to pursue advice through relevant directorial instigation or contact the Ministry of Environment in Islamabad (25).

2.2.2 Field work

These biosafety standards encompass all facets of field testing for genetically modified plants, animals, and microorganisms. Typically, all field ordeals should follow prior laboratory research. It is a customary practice that genetically modified organisms developed in the laboratory undergo field testing before any Introduction of products into the ecosystem for public use or distribution (26). The suggested field trials should include the following:

- Redo the trials conducted in the lab and verify the results obtained from laboratory examinations (27).
- Collect exact and reliable findings concerning the stability of genetically modified traits, their manifestation, and the passing on of these traits through generations in real-world conditions (28).
- Penalize the field credibility of genetically modified organisms, including factors such as their survival, reproduction, and competitive abilities (29).
- Assess the capacity of genetically modified organisms to adapt or evolve in response to varying environmental conditions (30).
- Assess the comprehensive environmental influence (31).

2.2.3 Commercial Release of Regulated Materials

These rules also describe the steps required to commercially deregulate controlled materials. As a standard practice, it is necessary to furnish comprehensive information from field trials to assess

whether the genetically modified organism or its resulting product is eligible for public approval or authorization. In this context, it is crucial to present all the information, factors, and data that formed the basis for the approval of commercial release in a different country (32, 33).

2.3 Guidelines for laboratory work

Four distinct biosafety levels are defined, each involving a combination of laboratory protocols and methodologies, safety gear, and laboratory infrastructure tailored to the specific tasks performed, the risk associated with the infectious agents, and the purpose or function of the laboratory (34).

2.3.1 Biosafety Level 1

Biosafety Level 1 practices, equipment, and facilities are appropriate for use in educational training labs at the undergraduate and secondary school levels, as well as in other facilities where the work involves well-characterized strains of live microorganisms that are not known to cause illness in healthy adults(35). Some examples of bacteria that meet these criteria are *Bacillus subtilis*, *Naegleria gruberi*, and the infectious canine hepatitis virus. It's important to note that many agents, while typically not associated with human disease, can still pose a risk to specific vulnerable populations such as young individuals, the elderly, or those with weakened immune systems(36). Therefore, assuming that vaccine strains, even if they have undergone multiple *in vivo* passages, are entirely non-virulent would be a mistake (37).

2.3.2 Biosafety Level 2

Biosafety Level 2 techniques, equipment, and facilities are suited to clinical, diagnostic, educational, and other facilities that operate with a wide range of indigenous moderate-risk agents found in the population and linked to varied degrees of human disease (38). Microorganisms classified at this containment level can be safely manipulated on an open laboratory bench using appropriate microbiological techniques, provided that the risk of generating aerosols is low. Some microorganisms falling under this category include the Hepatitis B virus, salmonellae, and *Toxoplasma* spp. Personnel working with these agents should be cautious about potential risks, including accidental self-inoculation, ingestion,

and exposure of the skin or mucous membranes to infectious materials (39). Procedures with a significant potential for generating aerosols that could expose personnel should be conducted within primary containment equipment or devices (35).

2.3.3 Biosafety Level 3

Biosafety Level 3 practices, equipment, and facilities are employed in clinical, diagnostic, teaching, research, or production facilities where activities involve indigenous or exotic agents, and there is a tangible risk of infection through aerosols. In such cases, the diseases associated with these agents can be severe or even fatal (35). Autoinoculation and ingestion are also major risks to those who work with these substances. *Mycobacterium tuberculosis*, St. Louis encephalitis virus, and *Coxiella burnetii* are examples of such agents for which Biosafety Level 3 protections are widely suggested (40).

2.3.4 Biosafety Level 4

Dealing with dangerous and uncommon materials that carry a substantial personal risk of causing life-threatening illnesses requires the utilization of Biosafety Level 4 procedures, safety gear, and facilities. Any activities involving potentially infectious diagnostic substances, isolated specimens, or animals infected naturally or through artificial means can potentially expose and infect laboratory staff. An illustration of a microorganism classified under Level 4 is the Lassa fever virus (34, 41).

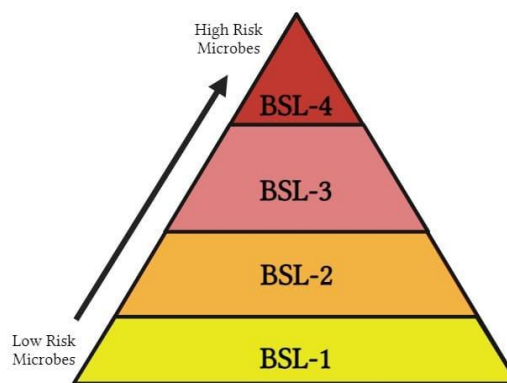


Figure 2: Biosafety levels (BSL) 1 to 4

2.4 Guidelines for genetically modified organisms (GMO)

2.4.1 Genetically modified microorganisms

When conducting fieldwork involving genetically modified microorganisms, it is essential to initially evaluate the characteristics of the biological system in question (42). This assessment can be summarized as follows:

- If the microorganisms have a track record of safe use in field settings, the work can proceed following the established standards for that particular microorganism (43, 44)
- These microorganisms originate from strains that have been previously documented in fieldwork.
- They perform the same functions as strains used in previously documented fieldwork.

The work is limited to locations and environments similar to past environmental circumstances and presumed to have a track record of being safely utilized. If the specified criteria are not met by the experimental microorganisms, the work can advance within suitable levels of containment (45). The proposed containment methods must meet one or more of the following criteria:

- Appropriate biological confinement occurs when Microorganisms are made non-replicable before conducting tests in the field; or Alterations are implemented to restrict the persistence of microorganisms beyond designated areas (46).
- Only in a specific location may genetically inserts and structures be swapped or transferred to other bacteria (47, 48, 49).
- There are physical systems established to contain microorganisms within the designated target areas or trial sites (50).

When dealing with microorganisms that have not previously been field-tested safely, the research can commence with the primary evaluation of risks to appraise the complete spectrum of plausible environmental consequences. Microbes identified as "problematic" in this assessment (51, 52) and engineered for the,

- Supporting the growth and nutrition of plant species, potentially providing an abundance of nutrients that could change the chemical composition of neighboring plants.
- Eliminating detrimental substances could lead to additional damage.
- Utilizing biological methods to manage plant pests that might outnumber the intended species, consequently generating harmful or disease-causing substances that can spread within the wild populations at the trial location.

2.4.2 Genetically modified plants

Before engaging in fieldwork involving genetically modified plants, one must initially contemplate the essence or qualities of the biological systems (53, 54), are as following:

- If experimental plants are believed to have a track record of safe field use, activities can move forward following the fundamental guidelines specific to the plant (55, 56). Plants that have been modified by ,Traditional breeding methods, such as Utilizing selective breeding, mutagenesis, protoplast fusion, or embryo rescue methods, and/or possessing innate traits or qualities common to conventionally bred plants (57). The incorporation of genetic inserts that are confirmed to be benign and pose no environmental risks is regarded as having a safe track record (58). Work may continue under suitable containment level and standards for experimental facilities that do not meet the condition (59). Containment measures must meet following requirements:
 - There is an absence of intermingling or crossbreeding occurring (60).
 - Precautions have been put in place to restrict the dissemination of plants and plant materials (61).
 - The expression of the introduced gene remains consistent and does not alter in response to shifting environmental conditions (62).

In the event of plants that have not previously been used safely in the experimentation (63, 64), the initiation of work can start by conducting an initial risk evaluation to establish, assess, and ascertain potential risks:

- The experimental site's ecological effects.
- Increased disease and pest resistance.
- A proclivity for gauntness.
- The impacts on other organisms, including both intended and unintended subjects.

2.4.3 Genetically modified animals

The following guidelines (65, 66, 67) should be followed when breeding genetically engineered animals:

- a. Genetically engineered animals must be raised in distinct breeding facilities that are easily identifiable as separate from non-engineered animals. Furthermore, genetically modified animals should be housed in separate facilities. If it becomes unfeasible to house them individually, small laboratory animals can be grouped for breeding purposes. The appropriate disposal of

- waste from genetically modified animals, including deceased specimens, should entail sterilization and, if required, incineration. When transporting genetically modified animals outside the designated workspace, containers with adequate durability and construction should be employed to prevent unintentional escape. Containers holding genetically modified animals should prominently display the phrase "Handle with Care" using distinct ink.
- b. Facilities, equipment, and other resources utilized in these studies should undergo performance testing during installation and regular assessments to maintain their original performance standards.
 - c. Each workspace should feature a sign indicating the presence of genetically modified animals.
 - d. Maintain a clean working environment.
 - e. Personnel working in these areas should exclusively wear work clothing.
 - f. When relocating genetically engineered animals to different facilities or persons, the responsible party must provide all relevant information to the receiving staff.

3. International frameworks and guidelines

It draws attention to the biosafety and biosecurity training obligations imposed on states parties by three international regulatory frameworks (68). Regarding each regime, the obligation to give evidence of conformity by reporting the existence of such provisions is reviewed. It claims that these technologies can be used to create and distribute complementary teaching and training resources for biosafety and biosecurity (69, 70, 71). It highlights how these building blocks can help life and related scientists better carry out their duty to protect their research from future exploitation by increasing their grasp of biosecurity risks (72, 73). It is undeniable that "global health governance" has emerged as a prominent concept on the global stage over the last 10-15 years, alongside the twin concepts of globalization and global governance (74). The World Health Organization (WHO) and the United Nations (UNAIDS, UNFPA, UNICEF, and the UN Economic and Social Council, among others) have both done work that has highlighted the importance of international cooperation and a common approach to global health oversight and monitoring (75, 76). By considering the World Health Organization's 2005 International Health Regulations standards for country biosafety and biosecurity implementation (69). Both the Biological Weapons

Convention (BTWC 1975) and United Nations Security Council Resolution (UNSCR) 1540 (UNSC 2004) allow States Parties to create overlapping frameworks for biosafety and biosecurity obligations (77). Combining responses to all three regimes by addressing biosafety and biosecurity together is of utmost importance. This cross-regime approach helps establish the education and training requirements for States Parties, both presently and in the future. Moreover, it fosters better compliance with all three regimes and, significantly, streamlines the reporting process (68).

3.1 International Health Regulations (IHRs)

The WHO International Health Regulations (73) have the primary goal of "preventing, mitigating, controlling, and responding to the international transmission of diseases"(78, 79). These regulations impose new responsibilities on State Parties, which extend to both domestic and foreign territories, covering a broad spectrum of public health scenarios that go beyond just infectious disease threats (80). As a globally applicable legal framework, the International Health Regulations of 2005 are binding on all 194 States Parties around the world, encompassing all member states of the WHO (81). The WHO questionnaire dispatched to States Parties in 2011 for the evaluation of their national implementation of the International Health Regulations (IHRs) is organized into 13 sections (82), each of the 13 sections in the WHO questionnaire addresses the eight essential capacities mandated for States Parties, which include coordination, legislation policy, surveillance, response, preparedness, laboratory, and human resource capacity. It also encompasses four specific hazard categories, which are zoonotic events, chemical events, food safety, and radiation emergencies, and concludes with points of entry (83). It also contains the following inquiries (84):

- Do individual laboratories have access to biosafety guidelines?
- Are there regulations, policies, or strategies in place for laboratory biosafety?
- Has an entity been assigned responsibility for laboratory biosafety and biosecurity?
- Have biosafety guidelines, manuals, or Standard Operating Procedures (SOPs) been distributed to laboratories?
- Are the staff involved adequately trained in biosafety guidelines?
- Has the categorization of microorganisms by risk group at the national level been completed?

- Is there an organization or individual responsible for inspecting laboratories to ensure compliance with biosafety requirements, which may include certifying biosafety equipment?
- Are biosafety procedures put into practice and subject to regular monitoring?
- Has a bio-risk assessment been carried out in laboratories to inform and update biosafety regulations, procedures, and protocols, including those related to decontamination and infectious waste management?
- Have diagnostic laboratories received official designation and authorization, or certification at Biosafety Level 2 (BSL-2) or higher, as needed for the relevant tiers of the healthcare system?
- Have national experiences and findings concerning biosafety been assessed, and have reports been shared with the global community?

3.2 United Nations Security Council Resolution (UNSCR)

Each of these sectors will require the necessary collaboration between various ministries, which will be encouraged and facilitated. On April 28, 2004, the United Nations Security Council (UNSCR) unanimously adopted Resolution 1540 (69, 84). States Parties acknowledge an obligation to abstain from the following: Engaging in actions outlined in Chapter VII of the United Nations (UN) Charter, and in accordance with UNSCR 1540, States Parties commit to refraining from:

- Supplying any form of assistance to non-state actors endeavoring to create, acquire, manufacture, own, transfer, or utilize nuclear, chemical, or biological weapons or their delivery mechanisms; (85)

And that:

- All nations must establish and enforce appropriate, efficient laws that forbid any non-governmental entity from producing, acquiring, owning, developing, transporting, transferring, or utilizing
- nuclear, chemical, or biological weapons, along with their delivery systems, especially for terrorist objectives. This should also encompass any efforts to partake in such activities, aid, or provide financial support for them (86)
- All countries should put into effect and uphold sufficient domestic regulations to inhibit the proliferation of nuclear, chemical, or biological weapons and their delivery systems, which should encompass proper oversight of related materials (69, 87).

3.3 The Biological Weapons Convention (BWC)

Under this Convention (83, 84), any State Party commits to refraining from creating, manufacturing, storing, or acquiring (88, 89):

- Microbial or other biological agents, as well as toxins, irrespective of their origin.
- Weapons, machinery, or means of delivery intended for deploying these substances or toxins for aggressive purposes or in warfare. This includes production techniques, types, and quantities that lack a valid rationale for prevention, protection, or other peaceful intentions.

4. Implementation of biosecurity and biosecurity measures

Biosafety involves the adoption of laboratory protocols and processes, the incorporation of particular structural aspects in laboratory facilities, the utilization of safety gear, and the establishment of suitable occupational health programs when dealing with potentially infectious microorganisms and other biological risks (69). These precautions are designed to safeguard laboratory personnel, the public, agriculture, and the environment from potentially harmful agents and other biological hazards. In recent years, there has been increased attention on laboratory-acquired illnesses (LAIs), particularly in laboratories with high (biosafety level 3, or BSL-3) and maximum (BSL-4) containment. LAIs can occur in various types of labs, including research facilities, clinical laboratories, or animal research centers, and it can be challenging to determine whether the infection originated in the lab or the broader population. LAIs also pose a significant public health concern, as an infected lab worker can transmit the infectious disease to colleagues, family members, or the wider community (90). Inadequate personnel training increases the likelihood of laboratory-acquired infections (LAIs) or other biological incidents in the laboratory. It can also result in improper handling, storage, and transportation of pathogens, which, in turn, could facilitate the unauthorized acquisition of biological

Table 1: Biosafety and biosecurity represent crucial foundations of global health security and are fundamental aspects of preventing the spread of biological weapons.

	WHO International Health Regulations (2005)	UN Security Council Resolution 1540 (2004)	Biological Weapons Convention (1972)
Applicability	All 192 UN Member States	All 192 UN Member States	163 States Parties
Purpose	“To prevent, protect, protect against, control and provide public health response to the international spread of disease ...”	To prohibit non-State actors from developing, acquiring, manufacturing, possessing, transporting, transferring, or using nuclear, chemical, or biological weapons and their delivery systems.	To prohibit development, production, acquisition, transfer, stockpiling, and use of biological toxin weapons
Requirements	8 core capacities “to detect, access, notify, and report events”	Domestic control to prevent proliferation of nuclear, chemical, and biological weapons, their means of delivery, and related materials	Any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition, retention, transfer, or use of biological weapons
Entry into force	15 June 2007	28 April 2004	26 March 1975
Mandated reporting/ where / when	Status of implementation / WHO/” As soon as possible but no later than five years from entry into force ...”	Status of implementation / 1540 Committee “Without delay”	None' "CBM voluntary reporting/ BWC ISU/ annually by 04715

agents by terrorists or individuals with intentions to engage in illicit bioterrorism or other criminal activities.

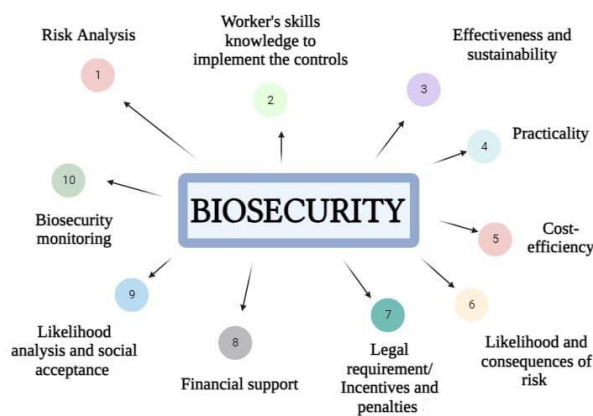


Figure 3: Analysis, designing and the steps of implementation of biosecurity

5. Challenges

Biosafety has become an increasingly important aspect of worldwide security, with broad-reaching consequences that impact various fields, such as healthcare, agriculture, scientific research, technology, education, and the armed forces. It constitutes a vital element of national security and deals with concerns such as concealment, rapid dissemination, accidental release, overflow, and the potentially devastating consequences of biological threats (91). To address biosecurity concerns, a rising number of study resources for biosecurity-related educational training have been developed and made available (73). For instance, the United Nations Interregional Crime and Justice Research Institute has founded the International Network on Biotechnology (INB), a worldwide coalition that includes academic research institutions, non-governmental organizations, international entities, and other stakeholders interested in promoting responsible



practices in the life sciences. The core objectives of this network are to raise awareness about both the potential advantages and risks associated with biotechnological progress, enhance education in responsible life sciences, and advocate for effective policies that ensure sustainable development in biotechnology. Notably, the INB is currently developing a digital platform that will enable the access, download, upload, and sharing of customizable educational and training materials, including technical briefings, case study videos, scenario-based exercises, and immersive learning experiences like virtual reality laboratory tours. The growing global need for improved disease diagnosis and control has led to an expansion of diagnostic and research capabilities. However, this increased capacity for detecting infectious diseases hasn't always been accompanied by a proportional enhancement of biosafety and biosecurity capabilities, especially in resource-constrained nations. Various obstacles impede the establishment or expansion of sustainable management capabilities for biosafety and biosecurity in these countries (92).

Despite of the presence of international initiatives and national regulations, concerns related to biosafety and biosecurity continue to exist. This underscores the necessity for enhanced cooperation between the scientific and policy sectors to foster a culture of safety and security within the bioscience community (93). In 2003, there were instances of laboratory-acquired SARS infections that took place within biosafety level 3 (BSL3) and BSL4 (the highest containment level) laboratories (94). As per a WHO investigation, these infections resulted from poor program management, including inadequate laboratory procedures and insufficient training. Likewise, even the most robust security measures can be compromised if the individuals with access to hazardous infections lack trustworthiness, reliability, and adherence to security protocols (72). Since 2003, there have been more than 100 biosafety and biosecurity incidents at laboratories in the United States, according to the Associated Press (95). Texas A&M University, for example, was fined \$1 million USD and had to cease all of its select agent research due to failures to adequately and accurately record events (96). Pirbright Laboratory in the United Kingdom unintentionally released foot-and-mouth disease virus into the neighborhood due to a leak in its wastewater pipes, which

were known to be in need of maintenance (97, 98, and 99).

6. Conclusion and Future Perspective

The study underscores the significance of national and international frameworks and norms in promoting the safe and secure handling of biological materials. These regulations play a crucial role in preventing accidents and mitigating risks associated with biological research and operations. Given the dynamic nature of biotechnology and emerging biological threats, continuous adaptation and global collaboration are essential. Adhering to these principles allows us to strike a balance between harnessing the benefits of biotechnology and minimizing potential threats to both people and the environment. The trajectory of future biosecurity and biodefense initiatives may be influenced significantly by the occurrence of the "next event." Nevertheless, the most likely scenarios involve events that unfold inadvertently and spontaneously, posing threats to human and animal health. These threats may emerge due to the development of new diseases or the resurgence of existing ones in response to changing environmental or cultural factors (100). In light of the substantial threats posed by evolving infectious diseases and bioterrorism, the responsibility for workplace biosafety and biosecurity extends to all individuals. However, the primary duty lies with governments globally, necessitating heightened awareness and readiness to detect and contain hazardous biological agents. This responsibility transcends the establishment of a safe environment solely for laboratory workers; it also involves the adoption of biosafety commitments. The well-being of laboratory personnel, the proper handling of pathogens, and the overall laboratory environment hinge on the implementation of secure and efficient laboratory procedures and pathogen management. These factors are pivotal in ensuring the successful completion of laboratory experiments. Acknowledgement: The author would like to acknowledge National University of Medical Science (NUMS), Islamabad, Pakistan and Kohat university of Science and Technology (KUST), Khyber Pakhtunkhwa, Pakistan.

Conflict of Interest The author has indicated that they have no competing interests or conflicts of interest.

Acknowledgments We are grateful to all the participants who willingly participated in the study.

References

1. Kumar S. Biosafety issues in laboratory research. *Biosafety*. 2012;1:e116.
2. Organization WH. Biorisk management: Laboratory biosecurity guidance: World Health Organization; 2006.
3. Callaway E. Biosafety concerns for labs in the developing world. *Nature*. 2012;485(7399):425.
4. Kumar S. Biosafety and biosecurity issues in biotechnology research. *Biosafety*. 2015;4(01):153.
5. Organization WH. Laboratory quality standards and their implementation. 2011.
6. Organization WH. Laboratory quality management system: handbook: World Health Organization; 2011.
7. Cembrowski GS, Carey RN. Laboratory quality management: QC [and] QA. (No Title). 1989.
8. Berte LM. Laboratory quality management: a roadmap. *Clinics in laboratory Medicine*. 2007;27(4):771-90.
9. Alexandrova N, Georgieva K, Atanassov A. Biosafety regulations of GMOs: national and international aspects and regional cooperation. *Biotechnology & Biotechnological Equipment*. 2005;19(sup3):153-72.
10. Khan T, Tanveer F, Muhammad J. Improving biosecurity in Pakistan: current efforts, challenges, and recommendations on a multidimensional management strategy. *Health security*. 2021;19(3):254-61.
11. Mugurusi E, Mwinjaka S. National Biosafety Framework for Tanzania: Regulatory regime on genetically modified organisms. The role of biotechnology in animal agriculture to address poverty in Africa: Opportunities and challenges. 2006:97.
12. Baumrind D. Principles of ethical conduct in the treatment of subjects: Reaction to the draft report of the Committee on Ethical Standards in Psychological Research. *American Psychologist*. 1971;26(10):887.
13. Khan S, Ullah MW, Siddique R, Nabi G, Manan S, Yousaf M, et al. Role of recombinant DNA technology to improve life. *International journal of genomics*. 2016;2016.
14. Jaffe G. Implementing the Cartagena Biosafety Protocol through national biosafety regulatory systems: an analysis of key unresolved issues. *Journal of Public Affairs: An International Journal*. 2005;5(3-4):299-311.
15. Falck-Zepeda JB, Zambrano P. Socio-economic considerations in biosafety and biotechnology decision making: The Cartagena protocol and national biosafety frameworks. *Review of Policy Research*. 2011;28(2):171-95.
16. Craig W, Tepfer M, Degrassi G, Ripandelli D. An overview of general features of risk assessments of genetically modified crops. *Euphytica*. 2008;164:853-80.
17. Vaccari DA, Strom PF, Alleman JE. *Environmental biology for engineers and scientists*: John Wiley & Sons; 2005.
18. Zohar D. A group-level model of safety climate: testing the effect of group climate on microaccidents in manufacturing jobs. *Journal of applied psychology*. 2000;85(4):587.
19. Potvin L, Cargo M, McComber AM, Delormier T, Macaulay AC. Implementing participatory intervention and research in communities: lessons from the Kahnawake Schools Diabetes Prevention Project in Canada. *Social science & medicine*. 2003;56(6):1295-305.
20. Council NR. *Biotechnology research in an age of terrorism*. 2004.
21. Bataw A, Kirkham R, Lou E, editors. *The issues and considerations associated with BIM integration*. MATEC Web of Conferences; 2016: EDP Sciences.
22. Jones MG, Fosu-Nyarko J, Iqbal S, Adeel M, Romero-Aldemita R, Arujan M, et al. Enabling trade in gene-edited produce in Asia and Australasia: The developing regulatory landscape and future perspectives. *Plants*. 2022;11(19):2538.
23. Burnette RN, Connell ND. Biosecurity challenges for the IBC: an exploration of the roles and responsibilities of institutional biosafety committees in the age of terrorism and biosecurity, now and for the future. *Ensuring National Biosecurity*: Elsevier; 2016. p. 185-200.
24. Aziz-ur-Rehman H, Mubeen M. Development and Progression of Regulatory Framework Associated With Seed Sector in Pakistan. *Dialogue (Pakistan)*. 2017;12(4).
25. Akmal T, Jamil F. Assessing health damages from improper disposal of solid waste in metropolitan Islamabad–Rawalpindi, Pakistan. *Sustainability*. 2021;13(5):2717.
26. Council NR. *Field testing genetically modified organisms: framework for decisions*. 1989.
27. Gniazdowski V, Paul Morris C, Wohl S, Mehoke T, Ramakrishnan S, Thielen P, et al. Repeated coronavirus disease 2019 molecular testing: correlation of severe acute respiratory syndrome coronavirus 2 culture with molecular assays and cycle thresholds. *Clinical infectious diseases*. 2021;73(4):e860-e9.
28. Gupta K, Karihaloo J, Khetarpal R. *Biosafety regulations of Asia-Pacific countries*. book. 2008:96p.



29. Snow AA, Andow DA, Gepts P, Hallerman EM, Power A, Tiedje JM, et al. Genetically engineered organisms and the environment: Current status and recommendations 1. *Ecological Applications*. 2005;15(2):377-404.
30. Kapuscinski AR, Nega T, Hallerman EM, editors. Adaptive biosafety assessment and management regimes for aquatic genetically modified organisms in the environment. Towards policies for conservation and sustainable use of aquatic genetic resources ICLARM (International Center for Living Aquatic Resources Management, Manila) Conference Proceedings; 1999.
31. Bayot ML, Limaïem F. Biosafety guidelines. 2019.
32. Akinbo O, Obukosia S, Ouedraogo J, Sinebo W, Savadogo M, Timpo S, et al. Commercial release of genetically modified crops in Africa: interface between biosafety regulatory systems and varietal release systems. *Frontiers in Plant Science*. 2021;12:605937.
33. Komen J, Tripathi L, Mkoko B, Ofosu DO, Oloka H, Wangari D. Biosafety regulatory reviews and leeway to operate: case studies from sub-Saharan Africa. *Frontiers in Plant Science*. 2020;11:130.
34. Council NR. Biosafety in Microbiological and Biomedical Laboratories. *Biosafety In The Laboratory: Prudent Practices for the Handling and Disposal of Infectious Materials: National Academies Press (US)*; 1989.
35. Zaki AN. Biosafety and biosecurity measures: management of biosafety level 3 facilities. *International journal of antimicrobial agents*. 2010;36:S70-S4.
36. Gallandat K, Lantagne D. Selection of a Biosafety Level 1 (BSL-1) surrogate to evaluate surface disinfection efficacy in Ebola outbreaks: Comparison of four bacteriophages. *PLoS One*. 2017;12(5):e0177943.
37. Manuaba AP. Prosedur Penggunaan Alat Perlindungan Diri dan Biosafety Level 1 dan 2. *Intisari Sains Medis*. 2016;6(1):117-23.
38. Barkham T. Laboratory safety aspects of SARS at Biosafety Level 2. *ANNALS-ACADEMY OF MEDICINE SINGAPORE*. 2004;33(2):252-6.
39. Andrade ACdSP, Campolina-Silva GH, Queiroz-Junior CM, de Oliveira LC, Lacerda LdsB, Gaggino JCP, et al. A biosafety level 2 mouse model for studying betacoronavirus-induced acute lung damage and systemic manifestations. *Journal of virology*. 2021;95(22):10.1128/jvi. 01276-21.
40. Mourya DT, Yadav PD, Majumdar TD, Chauhan DS, Katoch VM. Establishment of Biosafety Level-3 (BSL-3) laboratory: Important criteria to consider while designing, constructing, commissioning & operating the facility in Indian setting. *The Indian journal of medical research*. 2014;140(2):171.
41. Nisii C, Castilletti C, Di Caro A, Capobianchi M, Brown D, Lloyd G, et al. The European network of Biosafety-Level-4 laboratories: enhancing European preparedness for new health threats. *Clinical microbiology and infection*. 2009;15(8):720-6.
42. Tiedje JM, Colwell RK, Grossman YL, Hodson RE, Lenski RE, Mack RN, et al. The planned introduction of genetically engineered organisms: ecological considerations and recommendations. *Ecology*. 1989;70(2):298-315.
43. Sanders ME, Akkermans LM, Haller D, Hammerman C, Heimbach JT, Hörmannspurger G, et al. Safety assessment of probiotics for human use. *Gut microbes*. 2010;1(3):164-85.
44. Organization WH. *Laboratory biosafety manual: World Health Organization*; 2004.
45. Kimman TG, Smit E, Klein MR. Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures. *Clinical microbiology reviews*. 2008;21(3):403-25.
46. Shang L, Ye F, Li M, Zhao Y. Spatial confinement toward creating artificial living systems. *Chemical Society Reviews*. 2022;51(10):4075-93.
47. Herrero M, de Lorenzo V, Timmis KN. Transposon vectors containing non-antibiotic resistance selection markers for cloning and stable chromosomal insertion of foreign genes in gram-negative bacteria. *Journal of bacteriology*. 1990;172(11):6557-67.
48. Ali H, Hamayun S, Ullah M, Abbas M, Rehman M, Waleed A, et al. A Systematic Review: Clinical Manifestations of Diabetes Mellitus and The Role of Pharmacists in Management of Type II Diabetes. *Journal of Women Medical and Dental College*. 2023;2(1).
49. ur Rehman K, Khan SU, Zaman U, Saeed S, Rafique M, Ullah M. The Antibacterial Assessment of Biofabricated Magnesium Oxide Nanoparticles (MgO NPs) using *Conocarpus erectus* Leaf Extract: Antibacterial Assessment of Biofabricated Magnesium Oxide Nanoparticles (MgO NPs) using *Conocarpus erectus* Leaf Extract. *Journal of Women Medical and Dental College*. 2022;1(2).
50. Hopfield JJ. Neural networks and physical systems with emergent collective computational abilities. *Proceedings of the national academy of sciences*. 1982;79(8):2554-8.
51. Santos SR, Ochman H. Identification and phylogenetic sorting of bacterial lineages with universally conserved genes and proteins. *Environmental Microbiology*. 2004;6(7):754-9.
52. Zhou J. Microarrays for bacterial detection and microbial community analysis. *Current opinion in*



- Microbiology. 2003;6(3):288-94.
53. Conner AJ, Glare TR, Nap JP. The release of genetically modified crops into the environment: Part II. Overview of ecological risk assessment. *The Plant Journal*. 2003;33(1):19-46.
 54. Safdar M, Ullah M, Wahab A, Hamayun S, Rehman MU, Wazir MA, et al. Genomic Insights into Heart Health: Exploring the Genetic Basis of Cardiovascular Disease. *Current Problems in Cardiology*. 2023;102182.
 55. Aneja K. Experiments in microbiology, plant pathology and biotechnology: New Age International; 2007.
 56. Ullah SHM, Ullah N, Mahboob HA, Khan NU, Mehreen A, Waleed A, et al. Confidence and Accuracy in identification of adverse drug reaction (ADR) reported by inpatients. *International Journal of Basic Medical Sciences and Pharmacy (IJBMS)*. 2023;10(1).
 57. Van de Wiel C, Schaart J, Niks R, Visser R. Traditional plant breeding methods. Wageningen UR Plant Breeding; 2010. Report No.: 1566-7790.
 58. Bakshi A. Potential adverse health effects of genetically modified crops. *Journal of Toxicology and Environmental Health, Part B*. 2003;6(3):211-25.
 59. Adelman ZN, Pledger D, Myles KM. Developing standard operating procedures for gene drive research in disease vector mosquitoes. *Pathogens and Global Health*. 2017;111(8):436-47.
 60. Lübeck M, Poulsen H. UP-PCR cross blot hybridization as a tool for identification of anastomosis groups in the *Rhizoctonia solani* complex. *FEMS Microbiology Letters*. 2001;201(1):83-9.
 61. Thresh J, Cooter R. Strategies for controlling cassava mosaic virus disease in Africa. *Plant pathology*. 2005;54(5):587-614.
 62. Saleh-Lakha S, Miller M, Campbell RG, Schneider K, Elahimanesh P, Hart MM, et al. Microbial gene expression in soil: methods, applications and challenges. *Journal of microbiological methods*. 2005;63(1):1-19.
 63. Som C, Nowack B, Krug HF, Wick P. Toward the development of decision supporting tools that can be used for safe production and use of nanomaterials. *Accounts of chemical research*. 2013;46(3):863-72.
 64. Andow DA, Zwahlen C. Assessing environmental risks of transgenic plants. *Ecology letters*. 2006;9(2):196-214.
 65. McHughen A, Smyth S. US regulatory system for genetically modified [genetically modified organism (GMO), rDNA or transgenic] crop cultivars. *Plant biotechnology journal*. 2008;6(1):2-12.
 66. Cellini F, Chesson A, Colquhoun I, Constable A, Davies H, Engel KH, et al. Unintended effects and their detection in genetically modified crops. *Food and Chemical Toxicology*. 2004;42(7):1089-125.
 67. Turnbull C, Lillemo M, Hvoslef-Eide TA. Global regulation of genetically modified crops amid the gene edited crop boom—a review. *Frontiers in Plant Science*. 2021;12:630396.
 68. Beeckman DS, Rüdelsheim P. Biosafety and biosecurity in containment: a regulatory overview. *Frontiers in bioengineering and biotechnology*. 2020;8:650.
 69. Bakanidze L, Imnadze P, Perkins D. Biosafety and biosecurity as essential pillars of international health security and cross-cutting elements of biological nonproliferation. *BMC public health*. 2010;10(1):1-8.
 70. Dickmann P, Sheeley H, Lightfoot N. Biosafety and biosecurity: a relative risk-based framework for safer, more secure, and sustainable laboratory capacity building. *Frontiers in public health*. 2015;3:241.
 71. Ullah M, Wahab A, Khan D, Saeed S, Khan SU, Ullah N, et al. Modified gold and polymeric gold nanostructures: Toxicology and biomedical applications. *Colloid and Interface Science Communications*. 2021;42:100412.
 72. Maehira Y, Spencer RC. Harmonization of biosafety and biosecurity standards for high-containment facilities in low-and middle-income countries: an approach from the perspective of occupational safety and health. *Frontiers in Public Health*. 2019;7:249.
 73. Sun T, Song J, Wang M, Zhao C, Zhang W. Challenges and recent progress in the governance of biosecurity risks in the era of synthetic biology. *Journal of Biosafety and Biosecurity*. 2022;4(1):59-67.
 74. Wenham C, Busby JW, Youde J, Herten-Crabb A. From Imperialism to the “Golden Age” to the Great Lockdown: The Politics of Global Health Governance. *Annual Review of Political Science*. 2023;26.
 75. Bester A. Results-based management in the United Nations Development System: progress and challenges. A report prepared for the United Nations Department of Economic and Social Affairs, for the Quadrennial Comprehensive Policy Review. 2012;2730.
 76. Smith R, Blouin C, Drager N, Fidler DP. 11 Trade in Health Services and the GATS. A handbook of international trade in services. 2008:437.
 77. National Academies of Sciences E, Medicine. Dual use research of concern in the life sciences: current issues and controversies. 2017.
 78. Health WHODoM, Abuse S, Evidence WHOMH,



- Team R. Mental health atlas 2005: World Health Organization; 2005.
79. Organization WH. The World Health Report 2005: Make every mother and child count: World Health Organization; 2005.
 80. Rodier G, Greenspan AL, Hughes JM, Heymann DL. Global public health security. *Emerging infectious diseases*. 2007;13(10):1447.
 81. Ijaz K, Kasowski E, Arthur RR, Angulo FJ, Dowell SF. International Health Regulations—what gets measured gets done. *Emerging Infectious Diseases*. 2012;18(7):1054.
 82. Packer C, Halabi SF, Hollmeyer H, Mithani SS, Wilson L, Ruckert A, et al. A survey of International Health Regulations National Focal Points experiences in carrying out their functions. *Globalization and Health*. 2021;17:1-9.
 83. Razavi A, Collins S, Wilson A, Okereke E. Evaluating implementation of International Health Regulations core capacities: Using the electronic states parties self-assessment annual reporting tool (e-SPAR) to monitor progress with joint external evaluation indicators. *Globalization and Health*. 2021;17(1):1-7.
 84. Sture J, Whitby S, Perkins D. Biosafety, biosecurity and internationally mandated regulatory regimes: compliance mechanisms for education and global health security. *Medicine, Conflict and Survival*. 2013;29(4):289-321.
 85. Chapman TL, Reiter D. The United Nations Security Council and the rally'round the flag effect. *Journal of Conflict Resolution*. 2004;48(6):886-909.
 86. Russell JA. Peering into the abyss: Non-state actors and the 2016 proliferation environment. *Nonproliferation Review*. 2006;13(3):645-57.
 87. Cirincione J, Wolfsthal JB, Rajkumar M. Deadly arsenals: Nuclear, biological, and chemical threats: Carnegie Endowment; 2005.
 88. Huigang L, Menghui L, Xiaoli Z, Cui H, Zhiming Y. Development of and prospects for the biological weapons convention. *Journal of Biosafety and Biosecurity*. 2022;4(1):50-3.
 89. Millett PD. The Biological Weapons Convention: from international obligations to effective national action. *Applied Biosafety*. 2010;15(3):113-8.
 90. Bavoil PM. Federal indifference to laboratory-acquired infections. *Applied Biosafety*. 2005;10(1):5-7.
 91. Zhou D, Song H, Wang J, Li Z, Xu S, Ji X, et al. Biosafety and biosecurity. *Journal of biosafety and biosecurity*. 2019;1(1):15-8.
 92. Heckert RA, Reed JC, Gmuender FK, Ellis M, Tonui W. International biosafety and biosecurity challenges: suggestions for developing sustainable capacity in low-resource countries. *Applied Biosafety*. 2011;16(4):223-30.
 93. Gaudioso J, Gribble LA, Salerno RM. Biosecurity: Progress and challenges. *JALA: Journal of the Association for Laboratory Automation*. 2009;14(3):141-7.
 94. Artika IM, Ma'roef CN. Laboratory biosafety for handling emerging viruses. *Asian Pacific journal of tropical biomedicine*. 2017;7(5):483-91.
 95. Margasak L. Accidents on rise as more US labs handle lethal germs. Associated Press: October; 2007.
 96. Kaiser J. 'Texas A&M to pay \$1 million for biosecurity breaches. *Science Now*. 2008;20.
 97. Logan P. Final report on potential breaches of biosecurity at the Pirbright site 2007. Health and Safety Executive. 2007.
 98. Hse. Final report on potential breaches of biosecurity at the Pirbright site 2007. 2007.
 99. Inspectorate HF. Health and Safety Executive figures. London: HMSO; 1982.
 100. Ryan JR. Future Directions for Biosecurity. *Biosecurity and Bioterrorism*. 2016:345.

