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The Importance of Biosecurity in Emerging Biotechnologies and Synthetic Biology

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Abstract

The age of synthetic biology is ushering in new technologies for the advancement of society, human health, and agriculture. It appears that synthetic biology has integrated engineering paradigms into biological contexts. The combined use of new biotechnology and synthetic biology raises concerns about biosafety, biosecurity, and even cyberbiosecurity. For example, synthetic biology increases the possibility of designing, developing, and deploying pathogenic bioweapons in new and different ways than natural pathogens, as well as manipulating the genome. Evaluation of new technologies and platforms that enable creative or destructive manipulation of biological materials, systems, and organisms is important to identify potential security opportunities and vulnerabilities.

This issue poses challenges to the medical community and civilian populations worldwide, creating a growing need to implement and enforce standardized biosafety and biosecurity regulations to protect humans, animals, plants, and the environment. It is critical to establish rules and management guidelines, provide strong leadership at the individual and institutional levels, and utilize established biosafety and biosecurity tools to mitigate the risks associated with synthetic biology. This review addresses the current state of synthetic biology, focusing on the concepts of biosafety, biosecurity, and cyberbiosecurity, as well as enhancing the standardization, regulation, and management of biosecurity in synthetic biology.

In this review, the current situation in the Middle East region has been discussed and the challenges and opportunities encountered by synthetic biology researchers in this area is explored. The Middle East region is vulnerable to bioterrorism due to various factors. However, some countries in this strategically important region face challenges as they lack the necessary resources to effectively combat this significant global threat. These attacks are not limited to a specific border or area; they can affect multiple countries or have a global impact.

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Introduction

An introduction to the nature of the dual application of emerging biotechnology and synthetic biology

Synthetic biology is an engineering-based modeling and building techniques to modify existing organisms and modification of microorganisms with multiple applications [1] such as medicine (new vaccines, drug delivery, and treatment), and the modification of existing biological components such as DNA, bases, codons, genes, gene segments, and amino acids. It also emphasizes the creation of non-existent engineering biological components based on modern tools for faster and easier design, manufacture, and exploitation of genetically modified organisms [2,3]. Environmental improvement, energy (biofuels), and food production are also done in this field [4,5]. The distinction between the concepts of biotechnology and synthetic biology: Biotechnology is a broad term that includes the use of biological elements or processes to achieve human goals, while synthetic biology encompasses a range of ideas, methods, and tools of biotechnology that enable the modification or production of biological organisms [6]. Briefly, synthetic biology is the application of science, technology, and engineering to facilitate and accelerate the design, manufacture, or modification of genetics [7]. In recent decades, some European, American, and Asian countries have enacted laws and regulations to control the application of synthetic biology technologies in basic and applied research, which has brought some advantages [8]. On the other hand, due to the lack of strong laws in developing and violent countries, the techniques of this new biological system in emerging biotechnology and synthetic biology used to create dangerous pathogens, invasive organisms, or other destructive biological agents by individuals, terrorist organizations, or violent countries, and create potential hazards worldwide, especially countries with weak counter-terrorism capabilities [9]. This dual capability is called a Dual-Use Research area of Concern (DURC). Similar research techniques with legitimate scientific purposes can pose a potential biological threat to public health (including people, animals, and the environment) or national security if misused. Synthetic biology increases the possibility of designing, developing, and using pathogenic bioweapons in new and different ways from natural pathogens or other biological products [10]. Since infectious poliovirus particles were synthesized synthetically from chemicals using poliovirus cDNA in 2002, the scientific community has shown great importance to DURC [11].

Concepts of biosafety and biosecurity in emerging biotechnology

The concepts of biosafety and biosecurity are important in emerging biotechnology. Synthetic biology poses potential risks to biosafety and biosecurity [12]. These two types of risk can be differentiated. Biosafety involves ensuring the safety of individuals working in laboratories when handling microbes, cells, DNAs, or other biological products. Risks are not caused by intentional human mistakes, although these errors can pose the greatest threat to researchers, their labs, and society as a whole. Academic training, techniques, and proper equipment are essential in laboratories for safely handling potentially dangerous microbes and working with pathogens and biological products. Biosafety focuses on preventing and controlling unintentional or accidental biotechnology hazards and microbial biological events that are unintentionally induced [13,14]. Biosecurity encompasses preventive measures to mitigate intentional biological hazards. It includes areas such as national security, control of biological weapons, management of pandemic disease prevention, controlling their spread within populations or facilities, food security, prevention of invasive species, and containment or disinfection of infectious materials. Laboratory biosecurity encompasses more than just physical security; it also involves personnel management, material control and accountability, information security, transport security, and program management. In this subject, it is necessary to ensure the design and implementation of studies by the research company with access controls, physical security, and trusted workforces [15,16]. To ensure the safe and secure research and development of dangerous pathogens and biological agents, laboratories have controlled access, limiting admission to designated individuals only. This ensures that only authorized individuals enter the laboratory and limits access to pathogens or biological research and technologies to those who have received proper training, thereby minimizing the risks of technology or pathogen and biological agent's misuse. Attention should be given to fostering a safety culture and ensuring careful recruitment of personnel. This includes conducting background screenings and enforcing strict policies and procedures for laboratory access.

Biosecurity risks, as defined by the World Health Organization (WHO), include unauthorized access, loss, theft, misuse, diversion, or intentional release [17]. Biosecurity risks primarily stem from intentional and deliberate human actions [12,14]. Traditionally, naturally occurring pathogens in the environment, such as *Bacillus anthracis* (*B. anthracis*) and *Yersinia pestis* (*Y. pestis*), have been used as biological weapons due to their highly infectious nature, rapid transmission, and ability to cause widespread contamination. As synthetic biology continues to advance and expand its capabilities in creating and modifying biological weapons, there is a growing need to establish and enforce standardized biosafety and biosecurity regulations for the protection of humans, animals, plants, and the environment. Biosecurity is necessary to prevent, detect, and trace the origin of biological attacks to address the risks associated with the dual-use potential of synthetic biology [6]. A failure in either laboratory biosafety or biosecurity may affect the staff, community, and environment, and may endanger the institution's operations [16].

Biosecurity and the global challenge of disease outbreaks

Public health systems globally face constant challenges from various micro-organisms, particularly emerging and re-emerging viruses. Emerging and re-emerging infections, as well as potential acts of bioterrorism, pose ongoing challenges for the global medical community and civilian population [18]. Such events can range from the use of anthrax in terrorist incidents to global emergencies like the Ebola epidemics of 2014-15 and influenza pandemics [19,20]. The Asia-Pacific region, and at the top of them, the region of Vietnam, is recognized as an epicenter of Emerging Infectious Diseases (EIDs), of which 75% are zoonotic [21]. An EID caused by an unknown micro-organism poses a significant threat to global public health security and the global economy. It leads to numerous deaths across cultural, political, and national boundaries, as well as inappropriate economic consequences. Examples of acute cases include the coronavirus respiratory syndrome and the Middle East Acute Respiratory Syndrome (SARS) [22]. In these cases, a delay in pathogen diagnosis, considering the rise of global urbanization and communication, can result in social instability. These events and experiences have taught us valuable lessons. One important point is that high-control laboratories around the world collaborate and share their experiences to enhance their ability to respond to global threats. They play a crucial role in preventing and controlling highly infectious diseases. In the future, the most important factor contributing to safety and security in organizations will be trained and experienced employees. Therefore, it is necessary to develop a standardized training program [18]. Several international networks, such as the Global Outbreak Alert and Response Network (GOARN) of the World Health Organization, the Global Health Security Initiative (GHSI), and the Global Health Security Agenda (GHSA), are actively working to increase preparedness in emergencies and address potential challenges. These networks, along with others established by the WHO, are responsible for warning about the severe consequences of pathogens [18].

Effective governance and policy for biosecurity

Governance must strike a balance between the risks and benefits of emerging biotechnologies, which have both potential for misuse and potential for beneficial use in innovation and development. The potential for dual use and abuse is a global problem that demands careful attention from top policymakers. Unfortunately, biosecurity efforts are still incomplete due to the growing number of synthetic biology fields [23,24]. Modern technology is still regulated and secured by outdated laws, which is an insufficient strategy to ensure security in the future. Understanding scientific innovations, such as biotechnology, in the threat landscape necessitates the implementation of effective biosecurity measures to adopt 21st-century biotechnologies. Additionally, it is important to consider the structural vulnerabilities of these sciences and the potential causes of inadequate biosecurity measures. New biosecurity concerns arise from the wide range, increased accessibility, complexity, and uncertainty of current and future capabilities. Gene editing using CRISPR/Cas9 is a significant advancement in genetic engineering that has the potential to revolutionize human and environmental health research. However, it also carries the risk of causing significant and irreversible damage. Horizontal Gene Transfer (HGT) or Lateral Gene Transfer (LGT) is a use of gene editing that involves the movement of genetic material to rapidly spread a specific set of genes or alleles through a population. This process bypasses Mendelian inheritance laws and increases the likelihood of transferring the desired genes. Engineered gene drives are a promising new technology, but their ability to quickly change the genetic makeup of a population has raised concerns. Other potential negative consequences of gene editing include the uncontrolled release of gene-edited material into the environment, disruption of ecosystems by genetically modified organisms (particularly engineered gene drive systems), and unintended modifications (off-target) in genome editing. As an example of these activities, we can mention the distribution of a method using gene editing for the synthesis of horsepox in a laboratory environment [25]. Without an appropriate management system, these research activities could result in harm to humans, plants, and animals, as well as to natural ecological systems. Current international treaties, guidance documents, and national regulatory measures are designed to address potential harm caused by the dual-use property of synthetic biology. These include the Convention on Biological Weapons, the Convention on Biological Diversity the Model Code of Conduct for Biological Scientists (Tianjin Biosecurity Guidelines for Codes of Conduct for Scientists) [26].

Regulation and management of synthetic biology biosecurity in the international community

Synthetic biology has garnered significant attention from the scientific community and governments worldwide since its inception. Over the past decade, it has experienced rapid development. Since 2010, European and American countries have made substantial investments in synthetic biology [27]. In 2014, the European Regional Network for Synthetic Biology Research published the report "Towards a European Strategy in Synthetic Biology" (TESSY). However, due to the dual nature of synthetic biology, the international community has also shown significant interest in the potential biosafety and biosecurity risks associated with it, as well as the regulation of these risks [28].

One of the decisions made in this meeting is to conduct scientific on organisms, components, and products produced through synthetic biology techniques. These assessments will focus on the potential effects of these techniques on the conservation and sustainable use of biodiversity, to reduce biosecurity risks in communities. The connections between biodiversity and human health, as well as national biodiversity strategies, should be taken into account when preparing national biodiversity strategies and action plans, development plans, national health strategies, and the progress in the preparation of the State of Knowledge Review. The importance of the "One Health" approach in addressing the interconnectedness of biodiversity and human health is acknowledged. This approach recognizes the complex relationships between humans, micro-organisms, animals, plants, agriculture, wildlife, and the environment. It also acknowledges the relevance of the "One Health" approach in developing wildlife surveillance systems at the national and local levels, as well as strengthening national biosecurity measures related to bushmeat practices. The scientific community believes that biodiversity enhances capacity-building, technical and scientific cooperation, and other initiatives to support implementation. In 2013, three scientific committees of the European Union drafted scientific opinions on operational definitions, risk assessment methods, biosafety, environmental hazards, and research priorities in the field of synthetic biology. In October 2014, the 12th Conference of the Parties to the Convention on Biological Diversity adopted a decision on synthetic biology. This decision called for parties to establish and implement a risk assessment and management system that aligns with the Convention on Biological Diversity. The purpose of this system is to monitor risks related to biological safety and biosecurity [29,30].

Many biosafety conventions, protocols, and laws have been implemented, such as the World Health Organization Laboratory Biosafety Manual (WHO: 2020), the Federal Food, Drug, and Cosmetic Act (FD & C Act: 2006), the International Convention Plant Protection (IPPC: 1999), the WHO Guide to the Safe Transport of Infectious Substances and Diagnostic Specimens (1997), and the Convention on Biological Diversity (1992). However, none of these specifically address the prevention and control of safety hazards. Biology and synthetic biology have different focuses. Although experts and specialists in the field of synthetic biology have acknowledged the potential risks of biological safety and security, there is a lack of specific agreements, conventions, or laws that have been developed and approved to address the unique complexities and uncertainties of synthetic biology compared to other biotechnologies [28,31,32]. New risks in synthetic biology include wide access to technology, widespread dissemination of information, increased pathogen virulence, and the creation of new pathogens through synthetic biology and self-centered synthetic biology. Urgent formulation of specific regulations and policies is necessary for the security of synthetic biology [7,23,33,34]. However, in many countries and regions, synthetic biohazards are still subject to biosafety regulations and regulations for genetically modified products. However, these regulations often have loopholes when it comes to managing synthetic biology [28,35]. In the long run, scientists propose that launching the international Biosecurity Education network can improve biorisk Management [36].

The state of biotechnology and synthetic biology in Middle East countries

The Middle East region does not have clearly defined geographical boundaries. In the present context, it refers to a specific cultural region. Middle Eastern countries include Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Saudi Arabia, Syria, Turkey, United Arab Emirates, and Yemen [37] .

Middle Eastern countries have demonstrated a strong presence in the field of biotechnology, particularly in medicine and agriculture. Unfortunately, the Middle East region is currently facing numerous challenges that are causing significant concern both locally and internationally. These challenges include wars, armed conflicts, economic deterioration, political instability, public health issues, and a high number of refugees. These factors may increase the risk of infectious disease outbreaks and the potential use of biological weapons. This hinders the region's capacity to address biological hazards and potential threats. Biosafety and biosecurity measures should be promptly developed and implemented for these reasons. The current review of biosafety and biosecurity in the Middle East region found that certain countries in the region can prevent potential biological threats. According to research, Iran and Israel have the highest research and development budgets in the Middle East, each exceeding $2 million. Qatar and Saudi Arabia follow closely behind with budgets of $8 million [38] .The most commonly accepted biosafety level in the Middle East and other parts of the world is BSL-3, according to the biosafety level standards in Middle Eastern facilities. This finding is also evident in the safety equipment utilized in different laboratory activities, including drug discovery, foodborne pathogens, emerging pathogens, and toxins. The most commonly used Personal Protective Equipment (PPE) includes lab coats, gloves, face shields, and goggles. Some bacteria and viruses used in research require BSL-3 or BSL-4 lab coats for laboratory work. However, this raises the question of whether countries lacking the necessary BSL can effectively manage these pathogens, particularly during outbreaks. This situation emphasizes the significance of laboratories [39]. Israeli experts have found justification for the biological risks associated with GMOs and other biotechnology products, as well as the negative effects and unethical use of this research. This is evident from the regulations of Israeli bioethics committees, such as the Bioethics Advisory Committee of the Israel Academy of Sciences and Humanities [40]. Israeli researchers claim that they have not released GMOs in open fields because Israel exports mainly to the European Union, and the GMO issue in green biotechnology can cause concern among politicians. However, controversial red biotechnology issues are viewed as very straightforward in Israel, and there is no significant opposition from the Israeli public to this area of research and technology, which remains highly controversial in other parts of the Western world. Embryonic stem cells, human cloning research, and experimenting with human DNA for research purposes are not affected by the legislation [40]. Reproductive cloning is considered a serious violation of human rights by the international community (EP resolution on cloning of 1997) and "incompatible with human dignity" (United Nations Declaration on Human Cloning, March 8, 2005) [41].

Regulation and management of biosecurity in synthetic biology in Iran

Despite being classified as a lower middle-income country, Iran has a strong interest in biotechnology and has invested substantial funds in this field [38]. Many Iranian institutions, including the National Institute of Genetic Engineering and Biotechnology, the Pasteur Institute, the Razi Institute, and the Persian Gulf Biotechnology Research Center, primarily engage in biotechnology-related activities rather than focusing on research or commercial applications. Progress has been made in Iran in various fields such as recombinant proteins, recombinant drugs, animal cloning, stem cell technology, tissue engineering, and vaccine manufacturing [38,42].

Iran is currently prioritizing agricultural biotechnology to enhance crop quality and resistance to diseases and external factors. Cotton and rice plants are just two examples of transgenic plants that have been genetically modified to be resistant to diseases, insects, and drought. Creating new uses for palm trees is not only important for nutrition, but also contributes to the economy and climate balance in Middle Eastern countries like Iran. Genetically engineered baculoviruses are utilized to control the red palm weevil, the primary pest that impacts palm trees. Recently, Iran has implemented the highest biosafety standards in the cultivation of imported strawberries, resulting in a significant increase in off-season production. Tissue culture and biotechnology research centers and universities in Iran have also conducted genetic modification studies on strawberries [43,44]. In Iran, biological security in the livestock industry involves controlling biological agents in the environment and laboratories to prevent their loss, theft, misuse, unauthorized access, or intentional release. One of the challenges facing agricultural biotechnology in Iran is a lack of trust among certain individuals or politicians in this field. Researchers believe that the lack of scientific governance and national benefits-based approaches are the reasons for the significant inconsistency between Iran's capacities and achievements in biotechnology [45]. The responsibility for managing biological security incidents in the country or during biological attacks by the enemy lies with the country's biological defense headquarters [46].

Recommendations for Regulating and Managing Biosecurity in Synthetic Biology

Developing a top-down framework for controlling biosecurity risks in synthetic biology.

An effective framework is needed to manage the biosafety risks of synthetic biology at national, provincial municipal, and laboratory levels, for regulation and monitoring, and for a balance between maximum development and minimum dangers in this field [23,47]. The potential for a more "democratic" biotechnology capability accessible to any individual or group could also create new opportunities for accidental, unintentional, or deliberate misuse [48]. Concerning top-down governance measures for biosecurity, synthetic biology seems like a promising development. However, it also represents a potential source of instability in biological sciences, which could introduce new risks and regulatory challenges. Although synthetic biology appears to be largely protected by existing international and national regulatory systems, several creations highlight the limitations of top-down governance approaches that focus on prohibiting access to certain "inherently dangerous" scientific artifacts, which could potentially make the world less safe. In an era of synthetic biology characterized by technological convergence, increased access to biotechnological capabilities, and rapid growth of intangible bioscientific knowledge, finding the appropriate ‘mix' of top-down and bottom-up regulatory measures will require foresight, broad dialogue, and a willingness on the part of governments to explore new, hybrid forms of risk regulation [49].

Think tanks implement systems to control biosecurity risks

The regulatory framework will be effective with the participation of think tanks at all levels. Think tanks have various responsibilities in regulating and managing biosecurity risks. These include conducting risk assessments and keeping records, reviewing and monitoring risks, and implementing mitigation measures and precautions to address biosecurity risks. Assessing and recording the risk of synthetic biology is crucial, and grading the level of risk is essential. The levels of biosecurity in laboratories can be classified based on biosafety and biosecurity risk assessment. Risk review and oversight involve national-level think tanks comprised of provincial/municipal authorities and laboratory authorities. Finally, the three levels of regulation and governance (national, provincial/municipal, and laboratory) work together with experts and researchers to form an operational circle in practice. Risk precautions and mitigation measures are essential for assessing biosecurity risks when seeking approval from higher levels. The higher levels of the think tank should review amendments and proposals made by lower levels, regardless of previous approval. These revisions and proposals aim to enhance the safety of the synthetic biology laboratory. If approved, they will result in improved safety measures at a higher level [50].

Strengthen training and awareness on synthetic biology biosecurity among relevant personnel

Strengthening biosecurity and emergency training is crucial for synthetic biology researchers from diverse scientific backgrounds and personnel in companies involved in this field. Personnel should receive training on potential biosecurity hazards, prevention methods, and how to handle any problems that may arise. Scientists in the field of synthetic biology should be aware of the potential dangers associated with their research and be prepared to take immediate medical action in the event of a biosecurity emergency. A biosafety manual for synthetic biology laboratories helps ensure safe operations and biosecurity [19,51].

Standardizing synthetic biology

The issue of standardization in synthetic biology has significant implications at both technical and governance levels. In the first case, standardization in biology is expected to greatly enhance the potential of synthetic biology by making it more accessible, easier, and broader in scope, thus enabling us to manipulate and engineer life more effectively. Synthetic biology is a comprehensive engineering field that spans industries and electronics. As standards are prevalent in our technological society, the international community of researchers in the field needs to focus on standardizing biological parts, plasmids, and methods. The standardization of the biological realm is a challenging task [52].

Cyber biosecurity control is an essential aspect of security management

In recent years, with increasing access to technologies, cyber biosecurity and self-centered biosecurity (based on individual knowledge) can lead to synthetic biology biosecurity risks. Cyber biosecurity is an important emerging biosecurity issue. Since biological laboratory equipment is controlled and managed by the Internet, with increasing reliance on digital information and computing synthetic biology on servers and networks, operations have become increasingly vulnerable to cyber threats, such as unauthorized access, theft, and misuse of information. This creates an unprecedented cybersecurity problem in synthetic biology. Biosecurity risk factors, in turn, demonstrate the importance of managing and mitigating biosecurity risks [47,53,54].

Discussion

Biotechnological power is growing rapidly. The dual nature of emerging technologies and synthetic biology has led to progress in various fields such as science, technology, medicine, agriculture, and industry. However, it has also raised concerns about the potential threats of biological synthetic such as biological weapons. biological weapons threats include the increased ability to transfer pathogens between species and within species, the engineering of benign microbes to produce toxic compounds, the revival of extinct pathogens, and the development of resistance to treatment [55]. Biotechnology's rapid advancement, such as the decreasing time needed to synthesize DNA sequences, is leading to a future where DNA synthesis and other biological manipulations will be more accessible to small groups of technical experts.

Modern biological research and development, including genetic manipulations that enhance the lethality of certain viruses, pose inherent risks [56,57]. The main biotechnologies of interest shortly are expected to be oligonucleotide synthesis, DNA assembly (combining smaller fragments of oligonucleotides to create a larger sequence), genetic modification (editing and deletion), and targeted placement of desired sequences within the genome. Damage can occur when these techniques are used intentionally to disrupt human and environmental systems. The dissemination of information, techniques, or knowledge regarding the use of synthetic biology technologies for unethical purposes has facilitated their malicious use or abuse [25]. Concerns within the scientific community grew when a report was published regarding the development of genetically engineered *H5N1* viruses. These viruses, derived from pathogenic avian influenza (Highly Pathogenic Avian Influenza - HPAI) viruses, were discovered to be capable of transmitting among mammals through respiratory droplets [55]. The bioterrorist attack is considered the most significant threat to biosecurity in modern society. Surveillance and medical response are two essential measures for preventing bioterrorism. Biological warfare agents that terrorists may use to launch attacks include *Bacillus anthracis*, Brucella, *Rickettsia prow-azekii*, *Yersinia pestis*, and others [58]. These agents are primarily transmitted through airborne particles, food sources, or water. Bioterrorism is characterized by its infectious nature, ability to be concealed, simple production process, and wide-ranging effects. Anthrax spores have been selected as an ideal biological weapon due to their high lethality to both humans and animals. The demand for a rapid method of detecting anthrax spores is high [59].

The study of biological security has also become significant in other fields of synthetic biology. Due to a dangerous increase in the number of unregistered and unapproved "stem cells", biosecurity in stem research must be strictly controlled by international law. If not controlled, it creates social and scientific concerns that must be addressed when using Smooth Muscle Cells (SMCs) for cell therapy [60]. Biosecurity is significantly influenced by the ecology of animal and human populations, the biological characteristics of infectious agents, and management practices that impact interactions between hosts and agents. In addressing biosecurity, the response to various threats from zoonotic, foodborne, and emerging infectious diseases is considered [61]. Environmental conditions and human health are key factors contributing to national security, and governments have extended the concept of biosecurity to environmental biosecurity, linking it to the security of humanity, animals, and biological preparation to increase national security. In this regard, experts see damage as processes that hurt the ability of the ecological system to produce ecosystem products such as freshwater, food, and fuel sources and services such as pest control and disease control. Global ecological disturbance is perhaps the most under-understood security risk of the 21stcentury and both climate and broader ecological security risks remain under-understood as issues with present and tangible consequences for safety, security, and harm to ecological systems is an integral aspect of our definition of biosecurity [62].

Biosecurity in husbandry is a field that has gained increasing attention in the past few years from producers and veterinarians. The contentious nature of modern business conditions is another motivation for improved biosecurity, as do political and social pressures for improved food safety [21]. In synthetic DNA technology, rapid emergence is a key driver of innovation in medicine, biotechnology, and other fields. In the latest research, researchers found significant heterogeneity in security practices throughout the synthetic DNA technology industry, reflecting the current lack of standardized oversight for DNA synthesis [63]. In the cloning of some animals, despite observing placental abnormalities, prolonged gestation, fetal overgrowth, respiratory failure, poor postnatal survival, and ongoing poor health, some organizations like the UK Royal Society for the Prevention of Cruelty to Animals advocate against the use of cloning for farm animals, pets, and endangered species. Given that 22% of terrestrial vertebrates are threatened with extinction, some samples store vital genetic diversity in a viable state. The Convention on International Trade in Endangered Species (CITES) and the World Organization for Animal Health work to prevent trafficking and ensure biosecurity [64].

Accordingly, while targeted countermeasures can provide some level of protection, preventive measures are more effective due to the uncertainty surrounding the future of this field [65]. Biosecurity policies and practices must be updated to address the unique challenges posed by synthetic biology and the global, fragmented, and diverse nature of its threat landscape. Effective global biosecurity will not be achieved easily and may not be embraced by all national governments and non-governmental organizations. As a result, there is a high risk of misusing new biotechnology with unintended consequences [7]. The cross-border spread of hazardous biotechnological applications can have detrimental effects on local ecology, such as the removal or destruction of specific species through genetic engineering. It can also expose vulnerable human populations to irreversible consequences, with no possibility of recovery [66].

Concerning human embryonic research, in most countries where public policy has been adopted, research on human embryos or gametes is permitted under strict conditions. However, a few countries explicitly prohibit research on embryos by law, such as Austria, Ireland, Cyprus, Costa Rica, and Italy. Among the remaining countries surveyed, there is no explicit policy on embryonic research [67,68]. Tourism plays a crucial role in the exchange of biota; therefore, special attention has been paid to the relationship between tourism and the significance of biosecurity in the international community. Tourism could potentially become one of the most significant sources of biological pollutants on earth. Tourism (sometimes quite deliberately) can facilitate biological invasions through various factors such as the destinations visited, activities pursued, modes of transportation utilized, and other variables like aviation, rural and eco-tourism, the proximity of destinations to urban areas and other established destinations, heightened interaction between animals and humans, environmental alterations (*e.g*., road construction), and human exposure to infectious agents (*e.g*., mosquitoes) [69,70]. This is remarkable, given the scale of impacts that invasive species and diseases can have, along with the measures put in place to prevent them [71]. However, scientists have concluded that the complex set of institutional arrangements formed by these and other related measures for biosecurity has substantial gaps in its capacity to control and restrict biological invasions, particularly in the context of tourism, which faces broader tensions regarding sustainability [72,73]. The relationship between the economy and biosecurity is complex. In international politics and global health, there is an increase in the structures of the core perimeter. The society is not uniform; the poor in wealthy nations share some similarities with the poor in the periphery, including the lack of material resources and adequate healthcare services. Infectious diseases, such as Tuberculosis (TB) and HIV/AIDS, illustrate the relationship between economic deprivation and social diseases. To enhance the well-being and living conditions of marginalized populations, significant efforts have been made, such as reducing the cost of HIV drugs, developing new drugs for HIV, distributing innovative medical technologies in developing countries, and allocating billions of dollars from central regions to the periphery to improve public health. Humanitarian medical assistance and preventive medical interventions in remote regions aim to address issues before they escalate to the central areas [74].

For example, despite the successful eradication of polio worldwide by the WHO, the virus can be recreated in laboratories around the world by reducing the time required for genome synthesis, or the human influenza virus of 1918, which killed tens of millions of people worldwide, can be recreated [75]. Another example is the use of RNA interference, which allows researchers to turn off certain genes in humans or other organisms [57]. To ameliorate concerns about biosecurity risks, one approach is to design synthetic biology engineering components to live only on specific nutrients in synthetic biology laboratories and cannot survive outside the laboratory due to the absence of such components. This action can also minimize biosafety risks caused by unintended or unassessed releases or interactions between human-made and biological environments. This action should be enhanced by improving the regulation of the biosecurity risks of synthetic biology [76,77]. However, the fact is that addressing such actions due to intentional and malicious human intentions and the use of engineered components does not provide the necessary or sufficient conditions to eliminate the biosecurity risks of synthetic biology [7].

In 2020, Trump *et al* suggested that for 21st-century biosecurity, a resilience strategy based on prevention and recovery should be developed. This strategy requires three critical capabilities: 1) Development of cost-effective tools and techniques for passive and active detection of biosecurity threats, 2) Need for rapid diagnostic tools after threat detection to eliminate or manage the threat, 3) Need to strengthen intervention mechanisms that can eliminate or effectively contain the threat caused by the harmful engineering platform [78]. In December 2018, the WHO established a global, multidisciplinary expert advisory committee to examine the challenges associated with human genome editing (somatic and germline). This committee examines how best to promote transparent and reliable methods for developing a responsible and accountable governance framework for future applications of genome editing technology [51,54]. Now is the opportune moment to implement biosecurity measures to maximize the advantages of synthetic biology while minimizing its potential for dual use. This can be achieved by enhancing conditions, framing, prioritizing, and managing biosecurity risks, as well as mitigating cyber-biosecurity threats.

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Conflict of Interest

The authors declared no conflict of interest.

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