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The biological weapons threats and coping strategies for health promotion

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Abstract:

The biotechnology revolution and the emergence of new ways to change the genetic material of an organism have led to an increased risk of biological wars. Coping strategies against these threats is very important to improve the health of people. Therefore, due to the importance of this issue, this study is aimed to review the scope of using biotechnology and genetic engineering in wars and coping strategies in all over the world. In this review study, database includes of PubMed, Web of Science, Google Scholar, Scopus, and Science Direct were searched. The search was limited to reviewed articles in English published between 1990 and 2020. The primary search results generated 148 relevant references. After eliminating the duplicates and articles which were not related to the review of the abstract, 11 references were identified for inclusion in this review. Based on the results of these studies, the advances in genetic engineering can lead to the development of new weapons for other types of conflict and war scenarios, secret operations, and sabotage activities. Rapid developments in biotechnology and genetics have created environmental, ethical, political, and social challenges for many communities. Increasing awareness and sensitivity, monitoring, and building capacity for effective coping are essential. Biotechnology areas that will probably significantly contribute to countering biological weapons include recognizing the human genome, strengthening the immune system, identifying bacteria and viruses' genome, equipment for biological identification, new vaccines, new antibiotics, and anti-viral drugs must be monitored.

Keywords:

Biologic threat, biologic warfare, biotechnology, genetic engineering

Introduction

Today, biological threats make a great problem in all over the world.[1] From I ancient times, many methods used to kill or disability the enemies, i.e., some soldiers poisoned their arrowheads and water wells with natural materials.[1,2] In recent years term of genetic engineering is frequently used. Genetic engineering is human involvement in the process of gene transfer between biological organisms.[3,4] In the context of biological wars or bio-terrorism, it aims to manipulate the gene to create new pathogenic properties such as increased survival, infection, pathogenicity, resistance to drugs, etc.[4]

Although with advances in biology and biotechnology, it is expected to change the lifestyle of societies in this century, in parallel, with the misuse of biotechnology knowledge, it can lead to the generation of biological weapons using genetic engineering and threats caused by it. Today, the simulation and design of genes become routine news topics, many articles about biological warfare and bioterrorism caused by genetic manipulations are written and published.[5] The reality is that the new generation of biological weapons will create unpredictable positions using genetic engineering and pathogens generated by genetic engineering may form the next generation of biological warfare agents.[6]

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Based on available evidence, some countries are working on biological warfare factors through genetic engineering.[7,8] The development of modern biotechnology in medical and pharmaceutical research has led to the availability of knowledge and facilities all over the world.[9,10] Furthermore, classic biological factors can be produced even with the simplest genetic methods. The use of modern biotechnology has made it possible to create completely new and unknown biological weapons that, for technical or ethical reasons, may be used more than classic biological warfare agents.[11,12]

The spread of terrorist attacks and biological threats worldwide has made it necessary to recognize and prepare to face these events. Therefore, in this article, we have tried to investigate the new use of biological weapons made by genetic engineering and coping strategies to improve health of people.

Materials and Methods

In this systematic review article, we searched articles published in journals and available databases and libraries from 1990 to 2020 for this overview. Five selected popular databases that have more related articles such as PubMed, Web of Science, Google Scholar, Scopus, and Science Direct were searched with certain keywords include biological weapons, biological threats, biological disaster, biological emergencies, coping strategies, genetic engineering, and challenge. Included criteria were published with the English language on 1990–2020. Exclusion criteria were not available full text and not related to this topic. After conducting a comprehensive search for the relevant articles with our topic, the reference lists of the retrieved articles were searched for pinpointing the relevant documents. Finally, the EndNote software version X10 was used to manage the search library, screen duplications, and extract irrelevant articles. The searching strategy of PubMed was used as a model for searching other databases showed in Box 1.

Results

The primary search generated 158 relevant references. After eliminating duplicates, 101 articles remained. Then, 71 references not meeting inclusion criteria were excluded after further review and 30 articles included to studies. However, at the end among the papers, 11 articles were included in the study [Figure 1]. Based on the content analysis category and subcategory extract from selected articles. Selected references are mentioned in Table 1.

Data extraction and analysis

A descriptive and content analysis was used for analyzing the data because quantitative meta-analysis was not possible due to the heterogeneity of the results and the number of repeated or nonindependent samples. The primary synthesis of the studies was conducted separately for each of the included article formats. Then, descriptive and thematic analysis was performed for the included articles and literature reviews. Extracted the data from the included studies were checked by two authors for improving accuracy. Finally, ten themes were extracted from the studies [Figure 2].

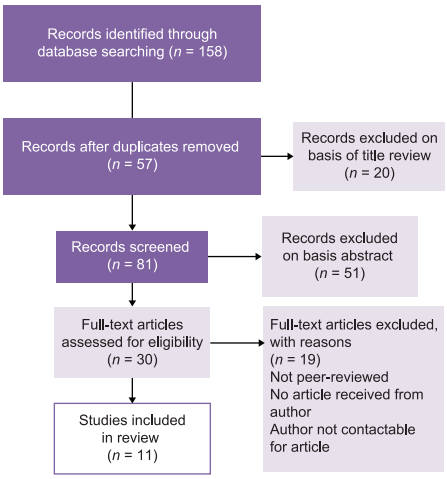

Figure 1: Flow chart of manuscript selection process PRISMA 2009

Keywords
Keywords relating to biological weapons
(((biological [Title/Abstract] OR "biological weapons" [Title/Abstract] OR "biological threats" [Title/Abstract] OR "biological emergency" [Title/Abstract] OR "biological disasters" [Title/Abstract] OR "biological emergency" [Title/Abstract] OR "biological event" [Title/Abstract] OR OR "biological accident" [Title/Abstract]))
Keyword relating to coping
(coping* OR "coping strategy" [Title/Abstract] OR "coping measurement" [Title/Abstract] OR "coping management" [Title/Abstract] OR "coping plan" [Title/Abstract] OR "coping planning" [Title/Abstract] OR "coping need" [Title/Abstract]))
Keyword relating to the health promotion
(health[Title/Abstract] OR "health promotion" [Title/Abstract] OR "health improvement" [Title/Abstract] OR "health progression" [Title/Abstract] OR "health enhancement" [Title/Abstract])
Limits: [Date of Publication:2020; English Language]

Box 1: PubMed search strategy

Understanding the human genetic structure

The human genome identification project has a profound impact on the speed of molecular biology research and helps solve the most mysterious and complex life processes.[21-24] Advances in biotechnology with the analysis of events that occur after infection with a pathogenic agent or the absorption of a toxic molecule in human body cells can clarify the conditions that cause the person to develop infectious diseases.[13,24,25] At present, the function of nearly half of the human genes is unknown.[22,24] The genomic studies, with the clarification of our unknown genes, will design new

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Table 1: Characteristics of selected studies

Reference	Title	Authors	Year published	Aim	Conclusion and recommendations
[6]	Genomics and future biological weapons: the need for preventive action by the biomedical community	Claire M. Fraser1 and Malcolm R. Dando	2001	Evaluate trends in genomics research and development and capabilities might be misused in the design of new bioweapons	The genomics revolution holds great promise for the advancement of basic biology, medicine and agriculture The threat of biological warfare and terrorism, though limited today, is real, and the genomics revolution has the potential to have major impacts on this most chilling threat during the 21st century
[4]	The biotechnology revolution: The science and applications	Nixdorff K, Brauburger J, Hahlbohm D	2000	Unclear	Biotechnology has since been revolutionized by molecular biology and genetic engineering, and any modern account has to take these developments into consideration
[5]	Synthetic biology and biosecurity: challenging the “myths”. Frontiers in public health	Jefferson C, Lentzos F, Marris C	2014	Show that the importance of tacit knowledge is commonly overlooked in the dominant narrative: the focus is on access to biological materials and digital information	Public discourse on synthetic biology and biosecurity tends to portray speculative scenarios about the future as realities in the present or the near future, when this is not warranted “Myths” play an important role in defining synthetic biology as a “promissory” field of research and as an “emerging technology” in need of governance
[13]	Directed evolution of proteins by exon shuffling	Kolkman JA, Stemmer WP	2001	Unclear	Developing in vitro formats for exon shuffling and applying these to the directed evolution of proteins
[14]	Gene mapping in the 20th and 21st centuries: statistical methods, data analysis, and experimental design	Terwilliger JD, Göring HH	2009	Review the theory and practice of gene mapping at the close of the 20th century	Propose a new focus in the field of statistical genetics that more explicitly highlights the primacy of study design as the means to increase power for gene mapping
[15]	Bioterrorism—preparing to fight the next war	Relman DA	2006	Unclear	Now is the time to begin making serious, sustained investments in the science and technology on which we can build agile defenses against an ever-evolving spectrum of biologic threats Recent investments in biodefense offer immense potential benefit, if guided by a creative, future-oriented perspective
[16]	Biological terrorism	Simon JD	1997	Unclear	By improving our readiness to respond to biological terrorism, many lives can be saved and terrorists denied their goal of creating panic and crisis throughout the country Trained to recognize the symptoms of diseases caused by biological warfare agents and have critical incident stress debriefing teams available to help them cope with the emotional aspects of treating exposed survivors should be part of contingency planning
[17]	Biological terrorism: understanding the threat, preparation, and medical response	Franz DR, Zajtchuk R	2002	Unclear	If done correctly, preparation for a biological attack will be as “dual use” as the facility that produced the weapon A sound public health infrastructure, will serve this nation well for the control of the disease, no matter what the cause of the disease
[18]	Emerging and readily available technologies and national security: A framework for addressing ethical, legal, and societal issues	Chameau J-L, Ballhaus WF, Lin H	2014	Articulates a framework for policy makers, institutions, and individual researchers	Merging and readily available technologies and national Security makes an essential contribution to incorporate the full consideration of ethical, legal, and societal issues in situations where rapid technological change may outpace our ability to foresee consequences

Contd...

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Table 1: Contd...

Reference	Title	Authors	Year published	Aim	Conclusion and recommendations
[19]	Field applications of genetically engineered microorganisms for bioremediation processes. current opinion in biotechnology	Sayler GS, Ripp S	2000	Unclear	Essential that field studies be performed to acquire the requisite information for determining the overall effectiveness and risks associated with GEM introduction into natural ecosystems
[20]	Closing loopholes in the biological weapons convention	Van Aken J, Hammond E	2002	Provides two examples of research that exploit perceived loopholes in the BTWC or impinge on the scope of the Convention	TWC or impinge on the scope of the convention, namely the planned use of biological agents for forced drug eradication and the development of anti-material agents

GEM=Genetic engineering microorganisms, TWC=Taylor woodrow construction, BTWC=Biologic taylor woodrow construction

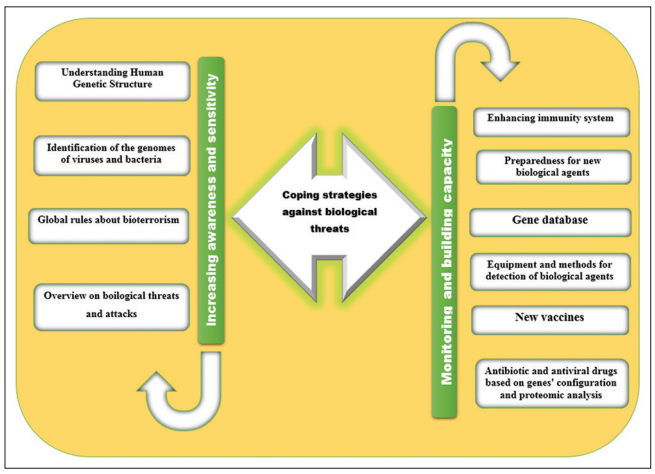

Figure 2: Coping strategies against biological threats

strategies for the prevention and treatment of microbial diseases based on created of vaccines and antimicrobial drugs.[5] Although there are reports of using biological agents to target specific ethnic groups.[5,6] According to theoretical opinion, ethnic cleansing is possible. However, most experts are uncertain about this possibility.[13,14,24,25] For the definition of racial groups, recognizing the sequence of the human genome has not yet created a genetic map. Various studies have shown that genetic variation in human populations is low in comparison to other species. Furthermore, there is more diversity within groups than between ethnic groups.[26,27]

Identification of the genomes of viruses and bacteria

The identification of microorganism's genome will determine pathogen characteristics such as pathogenicity or resistance to antibiotics.[28-30] By identifying microorganisms such as bacteria genomes, can modified them to produce biocontrols against the pathogen.[21] For example, E-coli can be used to produce commercial amounts of interferon, a natural protein with antiviral activity. On the other hand, it can create a genetically engineered bacterium that produces anti-pathogenic bioregulator agents.[21,22] Despite many benefits after identification viruses' genome, there are concerns about the production of secret viruses that are located only on specific genes. These secret viruses then activated by a stimulus and create a pre-designed disease or cause the programmed cell death.[23,24]

Global rules about bioterrorism

In many declarations and international conventions, using of biological agents on the battlefields has been banned. However, the unwritten rule of war may not follow these threats.[16,31,32] For example, several countries of signers, the Biologic Weapons Convention, such as Iraq (1972), have participated in illegal activities announced by the Convention. These events indicate the ineffectiveness of this convention as the only way to eliminate biological weapons and prevent them from spreading.[15,31-33]

Today, access to highly hazardous agents is increasingly restricted. For instance, smallpox, which was eradicated >20 years ago, is officially stored only in two high-security laboratories in the United States and Russia and it's now impossible to obtain the virus.[17,18,34,35] However, the rapid development of molecular biology provides possible to synthesize new compounds of this virus in the laboratory. For example, a research team at New York State University conducted a chemical synthesis of synthetic poliovirus. They were able to rebuild a complete virus using a genetic sequence of the virus that available online.[18,35] In fact, this method can be used to produce similar viruses that have a short DNA sequence. However, it should be noted that this method is complicated and only a few trained experts are likely to be able to do this.[16,17,34]

It seems that the most effective prevention of using such weapons is the fear of revenge and reciprocal use of similar methods. During the Gulf War, it is believed that Iraq was denied the use of chemicals in the war due to fear of retaliation.[15,31-33] However, this issue cannot

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always be honest, particularly nonstate terrorists cannot be easily prevented from committing these acts because biotechnology by using limited facilities create mass casualties.[30] However, the probability of terrorists with use biological agents made by genetic engineering is very low, but if an event occurs, its effects will be very obvious.[16,32]

Overview on biological threats and attacks

This despite the fact that molecular biology and genetic engineering are still at the beginning and more technical facilities will be created for military exploitation in the coming years.[5,6] Although the gene synthesis process was difficult and lengthy in the past, now, with the development of biotechnology, it is flourishing.[15,16,31-33] Today, quick and inexpensive methods have replaced the old.[17,18,34-38] The ability of attached specific viruses to the genome of specific populations at the desired time or to produce specific pathogens for specific groups clearly indicates the disturbing potential of the genetic engineering applied to the production of biological weapons.[5,6] There are also growing concerns about the incorrect use of biotechnology in agriculture and the misuse of genetic identity information of particular plant or human populations and manipulation of their safety systems. These processes can consider as bioterrorism attacks.[24] Genetic variation in human species is also a limited possibility to isolate small groups with exclusive genetic characteristics. In contrast, the genetic variation between plants and some animals can turn the food and agriculture industry into a simple and vulnerable target against biological attacks.[26]

Biological wars and bioterrorism are multifaceted problems that requiring hybrid solutions.[19,39] To solve bioterrorism problems that are constantly evolving, we must use the ideas of the best researchers and experts. Fortunately, similar advances in gene biotechnology that used to create biological weapons can be used to counter them. Probably, these areas of biotechnology will make a significant contribution.[20,39] However these weapons, in addition to will be really destructive, the possibility of their detection, prevention, and treatment have extraordinary challenges for many scientists.[23]

Preparedness for new biological agents

The genetic variation of classical pathogens is just a small fraction that new biomedical techniques have created. Based on military view, another very worrying problem is the creation of new types of biological weapons that there is no prior knowledge about them and as nonlethal instruments and not used in classical wars.[19,37-39] On the other hand, ignoring the global norms against biological weapons defined in Geneva today's technical facilities is creating a new challenge in this field that may lead to a new biological weapons race.[19,39]

One of the notable issues is using biotechnology to develop microorganisms that destroy substances. The idea is based on the fact that natural microorganisms are capable of breaking down any material, including plastics, rubber, metals, and chemicals.[20,39] This ability is now used to eliminate environmental contamination. Although this process is very slow and incomplete, it is possible to expand the performance of these organisms with genetic engineering to the degree that is sufficiently effective as biological weapons.[37,38] One of these genetically engineered germs can destroy military colors in 72 h and facilitate the destruction and degradation of aircraft by destroying their colors and coating.[19,20,39] Another similar study is the American effort to identify microorganisms that can destroy narcotics producer plants.[20,39]

Enhancing immunity system

The complete identification of the human genome sequence is an important issue for better identification and strengthening of the human body's immune system.[7] Furthermore, this process provides great potential and capability for coping with biological wars.[20] Based on the studies, research on mechanisms to strengthen the immune system has led to the identification of ways to protect humans against anthrax.[7,8]

Gene database: Advantage and disadvantage

In the past, limit access to pathogens was one of the ways to combat bioterrorism. But with the advance of DNA synthesis technology, just limiting access to dangerous pathogens does not lead to security.[28-30] Since the gene sequence is a plan, it can be synthesized without using the samples in the culture medium or stored DNA. Therefore, terrorists will not be able to build a genetic map without access to them.[27] It seems that limiting access to genomic databases can solve an important part of this problem. In fact, gene databases as one of the fundamental tools for researchers.[29,30,40]

The recent advances in gene sequencing are heavily protected and kept secret by governments in the gene databases.[15,31,33,40] However since medical science is widely published in the electronic and online database, gene sequencing data and DNA synthesis in some cases (such as smallpox, botulism, and anthrax) are published by and are available now in internet databases for free and unlimited.[27,28] This information can be used to simulate some microorganisms. For example, the Spanish influenza virus was spread in 1918, synthesized by a research team in 2000 and its genetic information has been published and easily accessible.[29]

Equipment and methods for the detection of biological agents

Regardless of whether microorganisms have been

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created through genetic engineering or not, scientists need to continuously advanced, rapid and automatic diagnostic tools for biologic agents.[5-7] According to comparing genomes with using DNA, which has already been possible, DNA microprocessors have been designed can identify the bacterial and viral genomes of the most important pathogens in humans.[6,41] This detector can identify genetic compositions of biological agents contain genes or plasmids such as antibiotic resistance or an artificial organism made from single genes.[41] Current detection methods can greatly reduce with using biosensors that have the ability to identify a biological factor in a quick and accurate manner.[6]

Be consider that today anyone with basic training can widely use ready-made and available kits to change the sequence of a gene or the displacement of genes in a microorganism. It can also spread viruses and microorganisms, providing small and disposable bioreactors.[29] The continuity of such progress equipment and methods for the detection of biological agents could reduce barriers to the development of biological weapons.

New vaccines

Vaccines stimulate the immune system to build antibodies against certain pathogens.[26,27] The availability of genetic sequences for many pathogens has led to the production of new vaccines against microorganisms.[28-30] Genetic engineering researchers are trying to create vaccines that stimulate the immune system against various diseases.[42,43] By using different antigens in a vaccine, a broad spectrum of immunity can be created. Although these methods have not yet been successful, recognition of antigens that are known base on the genetic sequence of pathogens is very valuable.[43]

Antibiotic and antiviral drugs based on genes' configuration and proteomic analysis

Progress in recognizing of the microbial genome has created great hope for the design of antimicrobial drugs.[4,5] Current antibiotics target three stages, such as replication, protein synthesis, and cell wall synthesis in germs.[4] The discovery of the codes of germ genes has made it possible to identify the viral proteins of the microbes and target them with broad-spectrum antimicrobial agents.[6] After the golden age of antibacterial drug production, decoding of viruses genome has now opened the way for the production of a new group of antiviral drugs by recognizing the pathogenicity and vulnerability of viral replication.[5,6]

Research on genes' configuration and proteomic analysis has led to the disclosure of a range of genes that are effective in pathogenesis and antibiotic resistance. Furthermore, it can speed up the misuse of genomic data. Some companies have developed methods in which break down genes into smaller pieces and create similar genes with new properties.[25] This technique will speed up the production of recombinant products up to twenty times faster. Although these methods are developed for industrial applications, they may be exploited.[13,25] Some scientists believe that the availability of human genetic sequencing will facilitate the development of biological weapons targeting specific ethnic groups. Although it seems very unlikely at the moment.[14] Although genetic predisposition to certain infectious diseases is a well-known issue, genetic coding is not the only determinant of susceptibility to the disease.[14,25]

Discussion

Based on the results from the review 11 article, we understand that biological weapon threat is old but ignored with many countries. The new vaccine, gene database, enhancing the immunity system, and other coping strategy is improving, but they have not yet reached the desired level. The advances in biotechnology knowledge allow the manipulation of microorganisms and the production of microbial agents with new features such as antibiotic resistance, change their antigenic characteristics and transmission of pathogenicity of microorganisms between agents.[1-5] Based on the results of some studies, manipulation of the classical elements of biological warfare makes it more difficult to isolate, identify, and cure factors and make them more suitable for military purposes.[5,6]

It is important to think about what will happen in the coming decades and when this revolution and genetic engineering development will spread globally. Today, concerning the creation of certain types of biological and mass murder weapons has been a global challenge.[22] Based on this review, concerns about biological threats and weapons are aggravated by the fact that the production of biological weapons is easy. Its raw materials, such as viral and bacterial plasmids, can easily be obtained from the scientists or their storage institutions. Then the release of genetic sequencing germs, makes it easy for the identification of genes that contribute to disease severity, adhesion to the host cell, immune response, and drug resistance.[11,12] Identifying the sequencing of pathogens genome can be a major contributor to the control and treatment of these diseases and can be exploited in the development of biological weapons.[11,12] We resulted from the initial search, that publication of genetic variation in human populations is low. Many countries in laboratories work on this variation for beneficial aim, but poor publication is accessible.[26,27]

At present, all military and civilian populations are exposed to biological weapons all over the world.

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Therefore, preparedness for responding to the biological agent's epidemic and genetic engineering is essential.[16,17,34] Nowadays, the use of genetic engineering in the future of biological weapons is not just a theoretical possibility.[31] On the contrary, it should be considered that any natural pathogens not appropriate for biological wars. Such factors include produced in large quantities, quick to operate, have good environmental compatibility, the resulting disease treated by the user and manufacturer of such weapons has a vaccine and the possibility of protecting insider soldiers.[32] These reasons explain why only a minority of natural pathogens are suitable for military purposes. In these cases, anthrax is the first choice to meet almost all of these factors. Based on specific characteristics of smallpox, such as very infectious and deadly and no effective treatment, this virus is an ideal biological weapon, especially for terrorist groups.[17]

Indeed, we can say that biological engineering and manipulation genomes have advantages and disadvantages. Advantage such as the production of antibiotics and antiviral drugs based on genes' configuration and proteomic analysis, new vaccines, and enhancing immunity system can create a great revolution in the promotion of human health.

Based on the results of Jefferson *et al*'s study in 2014, scientists need to continuously advanced, rapid, and automatic diagnostic tools for biologic agents.[5] This progress is very useful for people, but such advanced equipment and methods could reduce barriers to the development of biological weapons. Therefore, close global monitoring on these actions, is a necessary need in all over the world.

In all over the words, the gene database is challenging issues in recent years. Miller and colleagues mentioned in your research that recent advances in gene sequencing are protected and kept secret by governments in the gene databases.[40] Gene database is almost a secret resource and dose not let public access to this information. On the other hand, the publication of gene sequencing can be used to simulate some microorganisms that maybe had advantages and disadvantages effects on human life.

According to our search, few studies have examined strategies to coping with biological threats. One of the strengths of this study is the comprehensive review of all materials published around the world. However, due to the security issue of biological threats and events, many countries and research institutes do not publish their information and experiences and do not share them with other people. Therefore, this issue can be considered as a limitation for this study. It is suggested to conduct quantitative and qualitative studies with a large sample size and a survey of experts in this field.

Conclusion

The biotechnology areas that will probably significantly contribute to countering biological weapons include recognizing the human genome, strengthening the immune system, identifying bacteria and viruses' genome, equipment for biological identification, new vaccines, new antibiotics, and anti-viral drugs must be monitored. Companies need to obtain special licenses and permissions to enter the synthetic genes market must adhere to ethics and safety. Furthermore, customers of this technology and its products should be monitored.

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Conflicts of interest

There are no conflicts of interest.

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