Chapter 12
Safety and Security Regulations Against Biological Threats

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Abstract Biological threat agents include bacteria, viruses, fungi, parasites and their associated toxins. They have the ability to harmfully affect human health ranging from an allergic reactions to serious illnesses, even death. Water, soil, air, plants or animals can be a suitable habitat for their live and proliferation.

Because biological agents may reproduce rapidly and initially unnoticed, need minimal resources to survive and can infect at very small doses they can be used as biological warfare agent or bioweapon. Genetic modification may enhance their hazardous and lethal properties, or develop resistance to conventional treatments.

In effect, to protect people from dangerous biological agents as well as protect biological agents from intentional malicious acts both, biological safety and biological security measures should be implemented and respected. Because of wide scale of risks caused by biological agents, biosafety and biosecurity issues should be interpreted on many fields taking as priority protection of human beings and their surrounding environment.

The reader will familiarize with different point of views on biosafety and biosecurity issues in relation to occupational health and safety, public health and disease surveillance, biodiversity protection, genetic modification of microorganisms, transportation of dangerous goods, storage control of biological agents, dual-use technology, education and awareness raising, weapon of mass destruction threats and bioterrorism acts.

The main international agreements, the European Union regulations and principles supporting implementation of national legislation concerning biosafety and biosecurity areas are presented. The role of legally and not-legally binding instruments is highlighted, as well.

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12.1 Biological Threats

Biological threats contain biological material planned to be deployed to affect human community and/or environment providing human and animal diseases or else damage of plants [1]. Biological agents are sorted into three basic groups that would likely to be used as biological weapon – bacteria, viruses and toxins. Examples of high risk bacterial threats include among others anthax *(Bacillus anthracis),* plague *(Yersinia pestis),* epsilon (alpha) toxin of *Clostridium perfringens* and tularemia *Francisella tularensis)*. Examples of high risk viral threats includes influenza, coronaviruses (e.g. MERS and SARS), smallpox and Ebola virus. Examples of high risk toxins include botulinum neurotoxin and ricin. Moreover, biological agents comprise new and re-emerging pathogens as well as intentionally genetically modified infectious agents [2]. A biological threats are typically associated with the deliberate release of a biological agent in an act of terrorism. However, such threat can be a result from an accident in laboratory, as well.

The Valuable Biological Material (VBM), which includes biological agents requires administrative oversight, control, accountability and specific protective and monitoring measures in laboratories to maintain their economic and historical value and/or the population from their potential to cause harm. The VBM may include pathogens and toxins as well as non-pathogenic organisms, vaccine strains, food, genetically modified organisms (GMOs), cell components, genetic elements and extraterrestrial samples [3].

The diversity of biological agents and pathogens makes their management a significant challenge. In consequence both, biological threats and high consequence pathogens always deserve special attention.

12.2 Delivery Methods of Biological Agents

Contact transmission is the most common form of bacteria and viruses dissemination. There are two types of contact transmission: direct and indirect.

Direct contact transmission occurs when there is physical contact between an infected person and a susceptible person. Types of direct contact include both, (1) person-to-person interaction when an infected person comes into direct connection via touches or exchanges body fluids with someone else, and (2) droplet spread during coughing, sneezing and speaking, when droplets fall to the ground within a few feet and infect in close proximity.

Infectious diseases can also be spread indirectly, when there is no direct human-to-human contact. For example thru (1) airborne transmission, (2) con-

taminated objects, (3) food and drinking water, (4) insect bites or animals and (5) environmental reservoirs.

Some biological agents travel long distances and remain suspended in air for an extended period of time. Inhaling biological agents dispersed into the air (bioaerosols) may cause disease in people or animals indirectly, e.g. cold, influenza.

Furthermore, some microorganisms can live on objects for a short time. Mode of transmission via contaminated objects occurs when you touch an object such as a doorknob or bedding soon after an infected person, done it before you. It is high probability that you might be exposed to an infection, e.g. smallpox.

Infectious diseases can be also transmitted by food and water. *Salmonella* sp. is often transmitted through improperly handled produce or undercooked poultry meat. Improperly canned foods can create an environment ripe for *Clostridium botulinum*, which can lead to botulism.

Additionally, indirect spread of biological agents can happen in way from an animal reservoirs to vectors. Zoonosis occurs when disease is transferred from an animal to human. Zoonotic diseases include inter alia anthrax (from sheep), rabies (from rodents and other mammals), West Nile virus (from birds) and plague (from rodents). Besides, some zoonotic infectious agents may be transmitted by insects bites, especially those that suck a blood. These include mosquitos, fleas and ticks. The insects become infected when they feed on infected hosts previous, such as birds, animals and humans. The West Nile virus, Zika virus, tick-borne meningitis and Lyme disease are all spread by this way.

Moreover, soil, water and vegetation containing infectious microbes can also be transferred to human beings. Legionnaire disease is an example of a disease that can be spread by water.

In reference to biological attack and presented delivery methods our attention should paid unnatural pattern of disease transmission, reserve zoonosis spread (human to animals) or direct evidence of agents release. Based on that an appropriate prevention methods should be evaluated.

12.3 Definition of Biosafety and Biosecurity

Biological safety or biosafety includes measures aimed at protecting people and the environment from the unintentional impact of biological agents. It is rather related with prevention of incidental exposure, unintentional release, or accidental loss. Biosafety is mostly related to human, animal and plant health protection [4, 5]. Biosafety mostly relay on both, (1) occupational health and safety as well as (2) genetically modified organisms (GMOs) and biodiversity protection. Nevertheless, it also takes into account medical health care, epidemiology, agriculture, rDNA experiments, biosecurity and the Biological Weapon Convention (BWC) issues.

Biological security or biosecurity is much younger concept than biosafety [6] and comprises measures that minimize the possibility of biological agents being deliberately used to cause harm. It is rather related with prevention of theft and

unauthorized access, intentional misuse or diversion, dual-use issues, bioterrorism, intentional illegal release or criminal event. Biosecurity is more complex because has different associations in many contexts. From public health point of view biosecurity is much more related to security and oversight of pathogenic microorganisms and toxins in both, microbiology facilities and during transfer/transport. Biosecurity mostly is focusing on "protection, control and accountability for valuable biological materials within laboratories, in order to prevent their unauthorized access, loss, theft, misuse, diversion or intentional release [7]." In veterinary and agricultural sectors the biosecurity definition has come to denote protecting biological resources from foreign (not naturally occurring in this region, including genetically modified) or invasive species [8]. Moreover, biosecurity close corresponding to legal, regulatory and administrative measures export-import control of dangerous goods, facility-based biosecurity, security of clearance for personnel, intellectual rights protection, biosecurity of dual-use goods, crime investigation of biological threats, international agreements relevant for the non-proliferation of biological materials, equipment and technology (e.g. BWC, EU Green Paper, UN Resolution 1540), terrorism, state security issues, and of course biosafety subjects.

Both, biosafety and biosecurity are multi-source related and derived. Beside, defined in different ways by various authorities are always strictly related to biological agents [9].

During the Meeting of States Parties to the Biological and Toxin Weapons Convention (BWC) in 2003 the informal terms for biosafety and biosecurity were suggested. It was said that "Biosafety protects people from germs, and biosecurity protects germs from people [10]." Despite these definitions are informal, they present the merits of biological safety and biological security in up to the point and in easy way.

12.4 Legal Framework on Biosafety and Biosecurity

Legal framework on biosafety and biosecurity include both, legally and non-legally binding instruments.

Legally binding instruments carry the force of law and require signatories to comply with the agreements as adopted. This may include ratification, accession and/or transposition of agreements into national frameworks through implementation process. Legally binding instruments include international agreements and conventions, the European Union regulations and, different legal and constitutional arrangements in homeland legislations.

Compared with binding agreements, non-legally binging instruments do not create binding obligations and are not legal instruments enforceable by the national institutions. Consequently, there is no formal requirement to adopt them into national legislation. The advantage of non-binding agreements is being faster and simpler to adopt than binding agreements and providing more flexible means for update and adjustment. Non-legally binging instruments represent standards, guide-

lines, manuals, codes of conduct, good practices, recommendations and/or declarations, which are dealing with professional issue.

12.4.1 International Agreements and Conventions

International instruments regulating biosafety and biosecurity matters include treaties, conventions and agreements apply to most countries, but not always all. A number of existing agreements have been launched and implemented by UN agencies, although not all its members are signatories or parties of them.

The Convention on the prohibition of the development, production, and stockpiling of bacteriological (biological) and toxin weapons and on their destruction or biological weapons convention (BWC) is the first and the most important treaty banning the use of biological weapon and promoting biosafety and biosecurity on a global scale.

The Cartagena Protocol on Biosafety to the Convention on Biological Diversity (Cartagena Protocol) is addressing some environmental and health impacts of modern biotechnology. From biosafety and biosecurity point of view, the Protocol regulates an international transport and release of genetic modified organisms (GMOs) to protect natural biological diversity. The treaty was adopted in January 24–28, 2000.

The next one, the UN Security Council Resolution 1540 (Resolution 1540) passed in 2004, calls to all UN members to give high priority of joining and implementing the non-proliferation treaty regimes including the BWC.

Also, WHO International Health Regulations (IHRs) revised in 2005 represents a binding international legal agreement involving 196 countries across the globe. It aims to help State Parties in capability-building to prepare and respond to natural, accidental and intentional spread of diseases as well as to improve the BWC's Confidence Building Measures (CBMs) information exchange practice. Analogous to the Resolution 1540, the IHRs requires to consider and adopt both, biosafety and biosecurity regulations and practices.

12.4.1.1 The Biological Weapon Convention (BWC)

The first Article of the BWC presents the aim and scope of the whole treaty, namely, each State Party should take all necessary safety and security measures to protect the population and the environment as well as take into account scientific and technological achievements in the field of microbiology, genetic engineering, biotechnology, molecular biology and synthetic biology [11].

The biosafety concept is openly cited in the Article II, which requires States Parties to "destroy, or to divert to peaceful purposes" any biological weapons they have and specifies that in implementing this requirement "all necessary safety precautions shall be observed to protect populations and the environment [12]."

Biosecurity concept under the Convention is refered in Articles III and IV. The Article III calls State Parties to implement legal regulations in the field of transfer biological agents and measures indicated in the Article I of the Convention for peaceful purposes, including their security and protection during transportation [13]. The spirit of the biosafety and biosecurity concepts are evidently presented under the scope of the Article IV of the BWC, which stipulates Member Countries to take "any necessary measures [14]" to prohibit and prevention the proliferation of weapons of mass destruction (WMDs), encompassing according to the Final Declaration of the Sixth Review Conference legislative, administrative, judicial and other measures, including penal legislation. Through sentence "any necessary measures" should be also understood national implementation of the BWC, ensuring the safety and security of microbial or other biological agents or toxins in laboratories, facilities, and during transportation to prevent unauthorized access to and removal of such agents or toxins as well as education and raising awareness on BWC [15].

International consultation and effective cooperation of States Parties are a welcome tools for promoting biosafety and biosecurity practices, as well (Article V and VI of BWC [16].

The following, a mutual assistance and support of both, domestic agencies of State Parties and international organizations (e.g. WHO, INTERPOL, FAO, OIE, IPPC), in case of bioterrorism act suspicion or in response of any biological threat also will enhance global biological safety and security [17]. The Article VII promotes assistance in both, epidemiological and criminal investigations.

Finally, the possibility of using scientific knowledge for peaceful or malicious purposes reflects a dual-use dilemma and affects both, publication of knowledge and the biological agents themselves. Biosecurity from this point of view may be defined as a "balancing the promise of biotechnology with preventing the biological weapons threat [18]." The Article X of the Convention endorses cooperation of State Parties in transfer of knowledge and technology for peaceful uses of biological sciences. Therefore, it calls for closer institutional and educational cooperation between nations in order to improve protection of human and animal health [19].

Full implementation of the BWC is an important contribution to the fight against bioterrorism. Most, but unfortunately not all countries (Chad, Comoros, Djibouti, Eritrea, Israel, Kiribati, Micronesia (Federated States of), Namibia, Niue, South Sudan and Tuvalu) are signatories of the convention.

12.4.1.2 The Cartagena Protocol on Biosafety

The Article I of the Cartagena Protocol states that the main aim is "contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, bearing in mind risks to human health, and specifically focusing on transboundary movements [20]."

In brief, the Protocol promotes biosafety by establishing rules and procedures for safe trade of LMOs in order to protect natural biological diversity.

12.4.1.3 UN Security Council Resolution 1540

The Resolution 1540 (followed by the Resolution 1673 in April 2006) describes provisions for prevention of proliferation of nuclear, chemical and biological weapons. The main obligations are contained in the first three operative paragraphs including (1) prohibit States to provide "any form of support to non-State actors that attempt to develop, acquire, manufacture, possess, transport, transfer or use (…) biological weapons and their means of delivery", (2) to adopt and enforce (…) laws to prohibit such activities under their national legislation and (3) implement and enforce a comprehensive system of domestic controls on WMD and related materials [21].

In summary, the Resolution 1540 promotes biosecurity concept by establishing domestic laws for secure handling of biological material, physical protection of facilities where "high emergency pathogens" are located as well as border controls of biological material, means of delivery and dual-use items.

12.4.1.4 International Health Regulations

The main role of the IHRs, an international legal instrument drafted by the World Health Organization (WHO) is to enhance worldwide public health security. This role should be pursued through prevention, protection against, control and response to the international spread of disease, strengthen the collective defenses against the multiple and varied public health risks and finally, setting of rules to support the global outbreak alert and response system in order to improve international surveillance and reporting mechanisms for public health events, strengthen their national surveillance and response capacities.

Additionally, the WHO IHRs applies to all spectrum of public health risks, from natural disease outbreaks, new or re-emerging diseases, unintended consequences, then accidents, negligence, vandalisms or sabotages until deliberate use of biological weapon [22].

By adoption of the WHO IHRs, States Parties become more aware of the connection between public health and biological weapons reflecting closer integration the WHO and the BWC on biosafety, biosecurity, disease surveillance and reporting actions.

12.4.2 EU Legal Instruments on Biosafety and Biosecurity

Among regional instruments, the European Union (EU) legislation is one of the most extensive. The EU provides a common regulatory framework for biosafety and biosecurity issues mainly through directives adopted by the Council of the European Union and the European Parliament. All EU directives require implementation by EU member states through their national legislation. Therefore, the national

regulations on biosafety or biosecurity may look different in the EU countries, but ought to share a common minimum standard.

The most important EU regulations in biosafety and biosecurity fields are represented by both, the Directive 2000/54/EC on protection of workers from risks related to exposure to biological agents at work [23] and the Directive 2009/41/EC related to contained use of genetically modified microorganisms (GMMs) [24].

The Directive 2000/54/EC provides minimum requirements for occupational health and safety of workers exposed to biological agents beginning from the basic definitions in this field. Following, the Directive classifies the biological agents into four groups of threats based on the level of posted risk. It also provides information on how to prevent exposure to several groups of biological agents and limit the risk. Moreover, responsibilities of employers are described with respect to work involving (or likely to involve) exposure to biological threats. This Directive obligates each State Party to establish national provisions for carrying out surveillance of worker's health care prior to exposure and at regular intervals thereafter. The employer is obliged to ensure effective vaccines free of charge for his personnel. If a worker is found to be suffering from an infection or illness as a result of exposure at workplace, additional diagnostic tests should be offered similarly to other co-workers. Besides particular attention should be paid on suspicious presence of biological agents in human patients and animals, hazards represented by biological agents present in human patients or sick animals, and risks posed by the nature of the work. Appropriate decontamination and disinfection procedures should be implemented at workplace. Contaminated wastes should be handled and disposed without harm. Laboratories handling or use biological agents classified at 2, 3 or 4 group (according to the Article 2 and the Annex VI of the Council Directive 90/679/EEC) need to implement relevant containment measures in order to minimise the risk of infection.

As well as occupational safety systems, environmental protection needs to be considered in biological safety and security. Modern biotechnology is an emerging science with a great potential not only in improving human and animal health, ensuring the maintenance of biodiversity and environmental protection, agriculture, industrial and agricultural production, but also probability of using new scientific knowledge for malicious purposes. The EU has established a legal framework for safe and secure development of GMOs products based on both, (1) human and animal health, environmental protection, as well as (2) clear labelling and traceability of GMOs placed on the market.

The first one aspect, human, animal, and environmental health protection, is realized by the Directive 2009/41/EC on the contained use of genetically modified microorganisms (GMMs) [24], the Directive 2001/18/EC on the deliberate release into the environment of GMOs [25], the Directive (EU) 2015/412/EU on cultivation of EU authorized GMOs on their territory [26] and the Regulation (EC) 1829/2003 on genetically modified food and feed [27].

The Directive 2009/41/EC is the most important regulation on contained use of GMMs. In order to ensure a high level of GMMs protection, the containment levels (1–4 classes) and other protective measures should be used. Moreover, it recom-

mends using adequate safety and security measures in laboratories involving administrative procedures and/or notification requirements associated to the risk of the contained use of GMMs. The Annex IV of this Directive presents tables with minimum requirements and protective measures necessary for each level of containment. Additionally, it provides general terms related to this field and presents activities needed to be considered to develop risk assessment. In order to increase the flexibility for the amendment of the technical annexes, allowing timely adaptation to scientific and technical progress, the Commission may assist by advisory committees in necessity. Discussing further directives in this area goes beyond the scope of this publication.

The second aspect, the labelling and traceability of GMOs products is controlled by EU regulations, namely, the Regulation (EC) 1829/2003 on genetically modified food and feed [27], the Regulation (EC) 1830/2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms [28], to end with the Regulation (EC) 1946/2003 on transboundary movements of GMOs [29].

Additionally, protection of biological diversity is realized by various European agreements, including the Birds Directive [30], the Habitats Directive [31], the EU Biodiversity Strategy [32], the EU Forest Strategy [33] and the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) [34], etc.

Another aspect associated to biosafety and biosecurity measures is fact that infectious diseases may be easily spread and reach new regions. A legal agreements on border screening and control contribute to limiting transmission of infectious diseases in other countries. Many guidelines for transport of dangerous goods including safety and security elements have been translated by the EU into international acts and agreements that Member States were obligated to apply. The European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR) [35] classify infectious substances (Class 6.2) and provide secure measures for its transportation (general and specific requirements related to packed, labelling, marking of containers and vehicles, conditions of carriage, loading, unloading and handling, vehicle crews, equipment, operation and documentation, as well as construction and approval of vehicles). The Convention concerning International Carriage by Rail (RID) [36] provides regulations concerning safe and secure rail transport for dangerous goods. Also, the International Air Transport Association (IATA) consisting of 275 airlines, primarily major carriers, representing 117 countries priority is to ensure safety and secure shipments of infectious substances (certain principles, definitions related to biological agents, classification of infectious substances on A and B category (according to the IATA Dangerous Goods Regulations), list of indicative examples infectious substances in each category, packing instructions for infectious substances category A and B acceptable for air transport with a wide range of options for inner, outer and single packaging, labelling, conditions of carriage, loading, unloading, documentation, etc.), biological products, GMOs and GMMs, medical and clinical wastes, infected animals and patient specimens [37, 38]. Adequate regulations on safe and secure

transportation or shipment of dangerous goods or hazardous materials by water on vessel have been also established [39]. Additional directives related transportation of dangerous goods are presented below. Safety and security measures related to transport by road, rail and inland waterway are covered by the EU Directive 2008/68 on inland transport of dangerous goods [40]. Next, an uniform procedures for checks on the transport of dangerous goods by road and by rail are provided in, respectively, the Directive 2008/54/EC [41] and the Directive 2004/110/EC [42]. Safe transport of transportable pressure equipment by road and rail is included in the EU Directive 2010/35 [43].

Furthermore, dual-use nature of biological researches, equipment and processes also increase the likelihood of accidents involving high-risk pathogens. Efforts to strengthen biological security by reducing a threat posed by biological agents should require ingenuity and effective export-import control measures. The Regulation 428/2009 setting up a Community regime for the border control of exports, transfer, brokering and transit of dual-use items [44]. Additionally, the Australia Group (AG) supports associated countries to force export measures for control of dual-use goods. It provides control lists of potential dual-use materials including microorganisms and specific elements of specialist equipment dedicated for their large-scale production in bioreactors. The soft nature of this order make possible to update the catalogs by adding new items in response to actual threats. By actions focused on combating proliferation of chemical and biological weapons the Australia Group strengthen the BWC, as well.

In spite of biosafety, there is no legal framework for biosecurity in EU at the moment. This lack is replaced by international strategies, multilateral initiatives or actions organized and funded by EU [45].

One of the first primordial initiatives focused on the growing international security via Chemical, Biological, Radiological and Nuclear CBRN threats reduction policy was the EU Strategy against Proliferation of Weapons of Mass Destruction (WMD) [46] adopted in 2003. The Strategy identified probable ways of dual-use technology and knowledge misuse, which were considered to be "increasing as a result of rapid developments in life sciences". In reference to biological threats, the Strategy relied on all hazards of biological origin as well as highlighted the necessity to improve "the security of proliferation-sensitive materials, equipment and expertise in the EU against unauthorized access and risks of diversion [47]." This Strategy was updated in 2008. The same year, the European Council adopted a Joint Action 2008/307/CFSP [48], which supports the WHO's activities in the area of laboratory biosafety and biosecurity together with the above Strategy framework.

A one year before, in 2007, in order to reduce biological threats via one more way – enhancing preparedness and response activities, the European Commission had prepared the "Green Paper on biopreparedness [49]." This document arises from the consultation process on prevention, protection, prosecution of criminals/terrorists, surveillance, response and recovery aspects all relevant stakeholders represented by Member States and EU authorities. Summarizing, the discussions were focused on how to improve security and prevent of deliberate criminal acts, accidents as well as response to naturally-occurring outbreaks.

Subsequently, the above Green Paper and consultations made around it led to elaboration of the European Union CBRN Action Plan [50]. The EU CBRN Action Plan was intended to reduce a risk of public safety and security, and simultaneously, strengthen CBRN security in the European Union region. The EU CBRN Action Plan includes all hazard threats – from CBRN incidents of accidental, natural and intentional origin to terrorist acts, contributing the implementation of the EU Counter Terrorism Strategy [51]. In relation to enhancing biosafety and biosecurity, the CBRN Action Plan contains four specific actions – prevention, detection, preparedness and response – dedicated for high risk biological agents and toxins. Most of presented biological actions apply to preventive activities like the list of high risk biological agents and toxins (Goal 1 of the Prevention Chapter), enhancement of high-risk materials and facilities security (Goal 2 of the Prevention Chapter) and control (Goal 3 of the Prevention Chapter), participation of workers in the development of a high security culture at workplace (Goal 4 of the Prevention Chapter), improvement of identification, reporting, (Goal 5 of the Prevention Chapter), transport security (Goal 6 of the Prevention Chapter), information exchange (Goal 7 of the Prevention Chapter), provision of specific training (Goal 4 of the Actions applicable to CBRN prevention, detection and response Chapter) and personnel security (Goal 5 of the Actions applicable to CBRN prevention, detection and response Chapter).

No less important and also on the subject of biosafety and biosecurity on EU level is the Instrument for Stability (IfS) [52], which was established in 2006. One of its goal was contribution in capacity building against CBRN threats via full implementation of the BWC, strengthening biosafety and biosecurity capabilities according to the modern standards and providing trainings. In consequence of this initiative, the EU supports realization of several projects in Russia and Central Asia countries. In one of them, titled "Bio-safety and bio-security improvement at the Ukrainian anti-plague station (UAPS) in Simferopol" was engaged a Polish institution, the Military Institute of Hygiene and Epidemiology, which provided trainings in this fields [53]. From March 2014, the Instrument for Stability (IfS) was succeeded by the Instrument contributing to Stability and Peace (IcSP) [54].

One of the current conducting EU initiatives is the EU CBRN Risk Mitigation – Centres of Excellence (CoE) [55]. The rationale of it is promotion a culture of safety and security on chemical, biological, radiological and nuclear (CBRN) domains at regional level. The main interest of the CoE Initiative is building and/or enhancing national capacity to address CBRN threats in sensitive parts of the world themselves (mainly in five regions: African Atlantic Façade, Middle East, North Africa, South East Africa and South East Europe, Caucasus, Moldavia, Ukraine) in order to build a stronger EU security infrastructure.

The EU declared that supports and strengthens the BWC "national implementation measures, including administrative, judicial and criminal legislation, control over pathogenic microorganisms and toxins, (…) adoption of appropriate standards on biosafety and biosecurity measures (…) and development of national regulatory frameworks on biosafety and biosecurity [56]."

12.4.3 National Implementation

Based on the BWC provisions each State Party should "implement measures to minimise risks focus their national legislation, regulations and standards on safeguarding the workforce handling biological materials and on the protection of the environment, including the population, against accidental release or loss of hazardous materials. After 2011, (…) some State Parties focus their approaches on the physical protection of biological weapons-related biological materials to prevent unauthorised access by theft or diversion by non-State actors, including terrorists" [57]. An authoritative institutions or organizations may provide a support for states, how to create or enhance national biosafety and biosecurity system.

The Verification Research, Training and Information Centre (VERTIC) is an independent non-governmental organization (NGO), which supports State Parties in development, implementation and verification of international agreements related to disarmament, non-proliferation of biological and chemical weapons, and dual-use risks associated to biotechnology industry. At the Workshop on the Implementation of the Biological Weapons Convention, which was held in 3 August 2015 at Geneva, Mr. Scott Spence had presented a lecture on national implementation measures. He is a Director for National Implementation Programme and according to him the national implementation measures should include (1) definitions, (2) prohibitions and penalties, (3) jurisdiction, (4) biosafety and biosecurity, (5) transfer control and (6) enforcement issues. Regarding biological safety and security measures, he said that biosafety measures should mostly focus on prevention of unintentional exposure to pathogens and toxins or their accidental release. In contrast to biosafety, biosecurity measures need to concentrate on prevention of unauthorized access, loss, theft, misuse, diversion or international release of biological agents and toxins. Moreover, some specific biosafety and biosecurity procedures should be also established, specifically, a list of controlled biological agents and toxins, national system of notification about accidents, loss or theft, comprehensive record-keeping, physically secure of facilities, professional training on biosafety and biosecurity topics for personnel in addition to secure transportation for biological agents and dangerous goods [58].

Countries may choose different means of implementing internationally agreed principles through binding and/or non-binding national instruments. For this reason, there is a wide range of solutions that may be adopted at national level, including a variety of schemes, frameworks and instruments addressing to biosafety and biosecurity issues [59].

In the 7th Annual International Symposium – Biosecurity and Biosafety: Future Trends and Solutions, which was held in March 2016 in Italy, Mr. Scott Spence mentioned the latest Report on National Implementing Legislation [60]. According to the data included in the report many State Parties still need to strengthen their legal framework to ensure effective surveillance of activities related to hazardous biological agents and toxins. Many of countries involved at this Report should enhance biological safety and security by creation of independent supervisors,

develop procedures and policies for authorizing certain studies and related publications, meet the challenges of the biological weapons prohibitions posed by increasing availability of dual-uses agents, toxins, equipment and technology, and present biosafety and biological culture in all relevant communities by dedicated codes of conduct [61].

Apart from above, also other international organizations made efforts to present their suggestions regarding legislative or policy reforms in context to biosafety and biosecurity on domestic level. One of them is the United Nations Environmental Protection Biosafety Toolkit, according to which biosafety and biosecurity legislation should comprise (1) biosafety policy providing an overarching framework and clear principles; (2) a regulatory regime; (3) means to address notifications or requests for authorizations; (4) means for enforcement and monitoring; and (5) public information, education and participation mechanisms [62].

The safety and security systems against biological threats will be effective only, if will be implemented and fully respected at all levels of government – domestic law, regional agreements, general principles and international treaties.

12.5 Non-legally Binding Instruments

Owing to the fact that law is inherently conservative and usually works with lags to bioscience, which is accelerative, aggressively changed and rapidly evolving there is a real danger that law just cannot keep up. Moreover, with the passage of time, gaps between scientific risks and legal control may significantly widen.

As mentioned above, legally agreements and legislative measures provide an overall rules binding for each State Party. In contrary to them, non-binding instruments offer an advantage of being faster and simpler to adopt than binding agreements, and provide more flexible means for update and amendment. Moreover, in necessity, it is possible to put them directly into practice at once. This kind of opportunity offers standards, guidelines, manuals, codes of conduct, good practices, etc., which are usually published by specialized organizations dealing with narrow area of particular activity. Moreover, many international norms and regional legislations are based on existing biosafety and biosecurity standards. They are being developed with help of international organizations or NGOs dealing with dedicated issues directly, e.g. WHO – on global public health security, Food and Agriculture Organization (FAO) – in achieving food security, or World Organization for Animal Health (OIE) responsible for improving animal health worldwide, as well as authorizing institutions like European Committee for Standardization (CEN) and International Organization for Standardization (ISO). Some actions are conducted with collaboration, e.g. Global Health Security Agenda (GHSA) [63]. Other professional bodies also provide publications [64, 65] and freely available online resources in this field [66].

Specialized associations likeABSA International - The Association for Biosafety and Biosecurity promotes biosafety as a scientific discipline among biosafety pro-

fessionals, students and post docs, public health and hospital workers, emergency responders and scientists via development of professional standards, guidelines and regulations, providing training courses, webinars, conferences and workshops relevant to safe work, practices, lab equipment and instructional design of facilities [67]. The ABSA had been also active in biosecurity area for several years [68]. In similar way works the Asia-Pacific Biosafety Association (A-PBA) [69], the European Biological Safety Association (EBSA) [70] and the International Federation of Biosafety Associations (IFBA) [71].

Standards specified for biosafety and biosecurity management are dedicated for both, governmental and private institutions and following, are a helpful tool for State Parties for more effectively implementation of the international obligations in this field.

12.5.1 Biological Risk Management

Bearing in mind that the most probably exposition to potentially hazardous biological agents occurs in workplaces dealing with microbial agents directly, the WHO published some manuals strictly dedicated to laboratory personnel and health-care workers. One of them is a practical guidance on biosafety techniques for use in laboratories at all levels. The "Laboratory biosafety manual 3rd edition [72]" includes technical information on relation of risk group classification to biosafety levels (basic – Biosafety Level 1, basic – Biosafety Level 2, containment – Biosafety Level 3 and maximum containment – Biosafety Level 4) as well as laboratory type, laboratory practice and laboratory safety equipment. The Manual provides also types of personnel protective equipment, information of waste handling, accident reporting, laboratory animal handling, Standard Operational Procedures (SOPs), Good Laboratory Practice (GLP), safe collection and transportation of specimens for laboratory testing, secure transport of particularly dangerous pathogens, biosecurity activities in laboratories, codes of behavior, code of ethics for scientific research or codes of bioethics and so on. Besides, "Biorisk management: Laboratory Biosecurity Guidance [3]" consists of many specific aspects dealing with biological risk management and countering biorisk in biosecurity context, i.e. focusing on prevention of unauthorized access, theft, misuse, diversion or intentional release of agents and toxins from lab facilities.

To strengthening human health security by implementing the IHRs, WHO provides also other documents [73–75] and training courses associated to biorisk management (how to identify and control biosafety and biosecurity risks in laboratories, make a risk assessment or plan mitigation of risk, transport of infectious substances) [76]. Providing recommendations to specific present-day diseases or outbreaks also advance public safety and security [77, 78].

To set up requirements necessary to control risks associated with handling, storage and disposal of biological agents and toxins in laboratories and facilities almost

30 European countries agreed that an effective management system should be built. The concept of this system is based on a cycle of planning, implementing, checking, reviewing and improving performance and control of biorisk, which should be frequent upgraded. In result, the "Laboratory biorisk management standard [79]" presenting above concept was published as an effect of the CEN Workshop Agreement [80]. One more, the CWA 16335 describes biosafety and occupational measures as a professional competences for biosafety professionals, managers and trainers.

Likewise, the Office of Safety, Health and Environment of the US Centers for Disease Control and Prevention (CDC) in addition to the U.S. Department of Health and Human Services, the Public Health Service (PHS) and the National Institutes of Health (NIH) periodically update information and publish guidelines related to biosafety and biosecurity among workers in biological and medical laboratories [81]. Website promoting communication, transparency and awareness about biosafety, biocontainment, and laboratory biosecurity issues may be a good inspiration for finding the balance between Science, Safety and Security (S3), too [82].

12.5.2 Animal Safety and Security

Most of emerging infectious diseases are zoonotic and circulate in animal reservoirs before they cross over to infect humans. The response to all outbreaks of infectious disease is the same whether it is directed against naturally occurring infection, deliberate or accidental release. Many animal pathogens may be used as bioweapon because they have a high impact of infectivity, are cheap, easy to acquire, proliferate and unnoticed smuggled through border control. Moreover, molecular engineering of them may increase their virulence or make them more difficult to combat. In case of zoonotic disease coordination of both, animal health and public health officers is essential for quick diagnosis identification and confirmation, surveillance and the right trade of animals or products of animal origin. Control measures are often focused on eliminating a pathogen in the animal source.

The World Organization for Animal Health (OIE) collaborates in strengthening global biological security with many regional authorities and bodies. The OIE promotes reduction of health threats posed by animal-borne diseases through building a global surveillance and intelligence system for animal diseases and zoonotic situations, worldwide cooperation, policies, maintaining expertise and recommendations. It develops standards and guidelines to supports its Member Countries in protection themselves against transmission of diseases or pathogens during trade animals and animal products while avoiding unjustified sanitary barriers. The main objective of the OIE's standards is to recommend actions that will ensure biosafety and biosecurity via prevention of pathogenic biological agents transmission to animals, humans and environment [83].

In order to ensure adequate level of protection biosafety and biocontainment measures for veterinary laboratory workers handling hazardous biological materi-

als should be put into practice. A manuals of diagnostic tests and vaccines developed in collaboration with the WHO, provides not only a guidelines for establishing of laboratory biosafety, but also biocontainment measures focusing on prevention accidental or deliberate release of pathogens into the environment [84, 85]. The OIE contributes to ensure the safe and secure processes in facilities operational infectious animal agents thru setting out the management and technical competence for the testing accreditation zoonotic diseases, as well [86]. Further, the OIE develops and prints a codes, guides and manuals to help States detect and prevent spread of aquatic and terrestrial animal illness, including diseases related to biological weapons [87, 88].

Additionally, the International Veterinary Biosafety Workgroup (IVBWG) dealing with biosafety issues in high containment (BSL 3 and above) animal facilities had also developed a very useful handbook in this field [89].

12.5.3 Food Safety and Security

From biological safety and security point of view, the Food and Agriculture Organization of the United Nations (FAO) supports countries in protection of food security, as well as prevention and control food safety risks. The FAO had developed and published number of guidelines dedicated to actual microbiological threats in food. For instance, the "Biosafety Resource Book [90]," which is a result of the FAO's biosafety capacity development training courses organized from 2002 to 2010. The book provides biosafety regulators, policy-makers and members of national biosafety committees with reference materials that can be readily consulted beyond the training events, when the need arises.

The another one is the "Biotechnology for Agricultural Development [91]," which contains the proceedings of the FAO international technical conference dedicated to the Agricultural Biotechnologies in Developing Countries that was held on 1–4 March 2010 in Mexico. The major objective of this conference was to take stock of the application of biotechnologies across the different food and agricultural sectors in developing countries in order to learn from the past and to identify options for the future to face the challenges of food insecurity, climate change and environmental degradation.

In order to effective respond to food safety threats and reduce a food-borne risk, multiagency cooperation and state emergency response actions need to be launched. The FAO with collaboration with the WHO had identified and developed a framework for food safety emergency response plan ready for approval at national level [92]. The "FAO/WHO guide for application of risk analysis principles and procedure during food safety emergencies [93]" presents continuation and expansion of the aspect how to strengthening resilience to food safety emergencies at the country level. The next one assists countries in establishing and implementation of an effective national system for food safety emergencies [94].

12.5.4 Biodiversity Protection

Biodiversity or biological diversity is a variety of all living species on earth. It is include plants, animals, microorganisms, their genes as well as terrestrial, marine and freshwater ecosystems of their lives. Biodiversity is an important building element for many human goods and services, because is fundamental not only to our health, (clean air, fresh water, food products), but also provides products making our life easier.

The associations between biodiversity, biosecurity and biosafety are as complex as the ecosystems they create or protect. Biosafety generally is used to describe frameworks of policy, regulation and management to control potential risks associated with the use of new biotechnologies. Biosafety instruments address the risks posed to the environment and human health when LMOs or GMOs are released into the environment either for research (e.g. small-scale or field-testing) or for commercial purposes. Biosafety instruments and food safety instruments address, respectively, contained use of GMOs and the risks posed to humans by genetically modified foods.

According to the FAO, biosecurity encompasses policy and regulatory frameworks to manage risks associated with agriculture and food production. This includes introduction and release of LMOs and GMOs and their derived products, introduction and spread of invasive alien species, alien genotypes and plant pests, animal pests, diseases and zoonosis [95]. Similarly, according to Mrs. Lois Ransom from the Australian Government Department of Agriculture, Fisheries and Forestry, biosecurity in biological diversity context is defined as management of risks to the economy, the environment and the community of pests and diseases entering, emerging, establishing or spreading [96].

Various international, regional and professional organizations deal with biological safety and security in this field. For example, UN Environment Programme – Global Environment Facility Initial Strategy on Biosafety (UNEP-GEF) [97] assists in the development of National Biosafety Frameworks through information sharing, collaboration and capacity building initiatives at the regional and sub-regional level. Numerous training workshops and materials in this fields are available at UNEP-GEF Biosafety Projects web page [98]. Also, Organization for Economic Co-operation and Development (OECD) [99] covers biotechnology policies, bioeconomy, biosafety, intellectual property rights and a research programme on biological resources in agriculture areas. The both, the "OECD Best Practice Guidelines for Biological Resource Centres (BRCs) [100]" and the "OECD Best Practice Guidelines on Biosecurity for BRCs [101]" meet biosafety and biosecurity issues.

12.5.5 Transport

Owing to the fact that infectious diseases do not respect borders, biological agents represent a significant potential threat to public health. To limiting the spread of infectious diseases worldwide common standards for safe and secure transportation of biological agents need to be used in practice, as well. Lack of adequate border control may result social and economic consequences for states, regions or worldwide. In reference to this, WHO had prepared and published a guide on transport of infectious substances [102]. It provides information for classifying infectious substances for transportation by all modes of transport and ensuring their safe packaging based upon levels of risk. Moreover, in order to provide protection and expeditious transport of these materials a good communication between the sender, the carrier and the receiver should be maintained. This guidance is regularly updated including the changes that apply each year.

Moreover, transport of dangerous goods related to nuclear, chemical and biological weapons by road, rail, inland, waterway and air is covered by numerous guides developed by many organizations specialized in transportation [103–107]. Some of them provide also trainings and publications available on their web pages [108].

Today, many of guidelines for safety and secure transport of dangerous goods had been translated into laws or binding regulations and put into practice [109–112].

12.5.6 Dual-Use Nature of Biological Researches

The possibility of using bioscientific knowledge for peaceful or malicious intention shows the dual-use dilemma [113] and affects both, publication content and biological materials themselves. The obvious point is that in order to learn how to defeat any disease we need to learn how it mechanism works. Thus, at the core of research dedicated for protection against biological violence is a paradox because methods that generate life-saving improvement (vaccines, treatments, etc.) are the same methods that could generate catastrophic damage. Some say that biosecurity is balancing the promise of biotechnology with preventing the biological weapons threats [18] and the efforts to strengthen biosecurity and reduce the threats posed by biological weapons require moral and ethical responsibilities of life scientists.

Obviously is fact that any crime should be punishment by law, nevertheless, in order to do it we need to specify what kind of scientific activities – methods or techniques should be forbidden. It is impossible if we use the same techniques and reagents for both. Moreover, there is lack of devices would detect unlawful take biological agents out of lab facility. Therefore, only thru building individual responsibility of themselves and our nature we can stimulate a conscience of scientists to consider pro and con of their achievement's application. We can raise their aware-

ness on biosafety and biosecurity issues though education scientific community about the nature of the dual-use methods in biotechnology, reviewing plans for experiments or detailed methodology of sensitive publication, ensuring a role of life sciences in efforts to prevent bioterrorism and biowarfare.

Ethical codes and codes of conduct are primarily awareness-raising tools to remind scientists that they should contemplate potential consequences of their research. Such codes can also play a role in undergraduate and postgraduate education as part of education program in order to prepare students to think consequences of their activities, including any likely side effects. The content of codes of conducts usually involve fundamental issues such as awareness, safety and security, education and information, accountability and oversight. By biological safety and security should be understood the fact that scientists working with infectious agents such as natural or synthetic pathogens or dangerous toxins must be responsibly for use good, safe and secure laboratory procedures, whether codified by law or common practice [114]. They could also provide frameworks or guidance how develop a response to particular discoveries.

The *Biosecurity Working Group* under the *InterAcademy Panel* (IAP, The Global Network of Science Academies) [115] is a global network of the world's science academies, whose goal is to join forces to advise citizens and public officials on the scientific aspects of critical global issues. The IAP bringing together biosecurity experts from many countries in the world (inter alia USA, Canada, China, Australia, Poland, Nigeria, Cuba, Egypt, United Kingdom and Russia) also promote good biosecurity practices among scientists. The IAP Biosecurity Working Group is a regular participant of both, the BWC Meeting of Experts and the BWC Meeting of State Parties, where presents actual implications of scientific research for the BWC and biosecurity [116]. Most of ethical codes were developed and published aftermath discussions the IAP Biosecurity Working Group with close cooperation of scientific and international community [117].

Moreover, during the Eighth Review Conference of the BWC, European Union underlines the risks and threats posed by the rapid advances in biological science, including the possible acquisition and development of a biological weapon by a terrorist group [118]. Also the two intersessional meetings (2003–2005 [119] and 2007–2010) had engaged academic research communities and industry, partly in an effort to explore biological threat reduction options through discussions and consultation on biosafety, biosecurity, disease surveillance, response and other policy and procedural mechanisms.

Apart from that frequently are organized symposiums, conferences or workshops during which different approaches and perspectives of how to regulate subjects related to the Dual Use Research of Concern (DURC) are deliberated, mainly focusing on microbes and raising connections to them concerning on biosafety and biosecurity issues or potential limits to the freedom of research [120].

12.5.7 Bioterrorism

Lots of natural occurring pathogens or toxins could be used for warfare or terrorism. The idea of using microorganisms as warfare agents has a very long history [121–124]. Over the years many international authorities dealing with counter threats of biological warfare came to the common conclusion that (1) more intensive cooperation for threat assessment and planning as well as (2) implementation of national legislation in line with the BWC may significantly reduce this kind of threat.

In development of the bio-preparedness plan or strategy should be involved not only policy makers, law enforcement, medical doctors or customs officers, but also any other relevant national agency representatives working in the area of bioterrorism, who will be or potentially may be engaged in prevention, protection, first response capacity, prosecution of criminals or terrorists, surveillance, research capacity, response and recovery aspects [125]. Cooperation among different sectors represented not only national, but also regional or international level may allow to develop a coordinated national prevention and response plan dedicated for biological terrorism.

The CDC had developed a system to prioritize biological agents according to their risk to national security and categorize them. The Category A agents includes the highest priority bioterrorism agents such as *Bacillus anthracis, Clostridium botulinum* toxin, *Yersinia pestis, Francisella tularensis* as well as variola major, filoviruses and arenaviruses. Following, the Category B agents are moderately easy to disseminate and result in low mortality. These include *Brucella* sp., *Burkholderia mallei, Coxinella burnetii, Rickettsia prowazekii* and other agents. And finally, the Category C agents involve emerging disease agents that could be engineered for mass dissemination in future, such as Nipah and hantavirus [126].

Strengthening public-health care and infectious disease medical infrastructure, adequate epidemiologic and laboratory capacity with high biosafety lab levels, rapid detection, identification and characterization of the agents, effective disease surveillance, emergency distribution of antibiotics and vaccines, secure collection of traces at the crime scene, border control, training of multi-agency response and communication systems during simulation of similar events are some of steps contribute for biodefence capability-building [127].

Furthermore, deliberate contamination of food is also a real and still actual threat, which may have global public health implications. Member States of WHO had expressed concern that chemical, biological or radio-nuclear agents might be introduced into food and other media to intentionally harm people many times. That is why, WHO had published some guidelines with technical information how to prevent and respond to intentional contamination of food. The first one “The Public health response to biological and chemical weapons: WHO guidance [128]” had been revised and published in 2004. This second edition of WHO’s 1970 publication “Health aspects of biological and chemical weapons [129]” includes information designed to guide preparedness for and response to the deliberate use of biological and chemical agents that affect health.

Secondly, after 2008, WHO issued an update to the 2003 original guidelines "Terrorist Threats to Food – Guidelines for Establishing and Strengthening Prevention and Response Systems". This book responds to increasing concern in WHO's Member States that chemical, biological or radio-nuclear agents might be used deliberately to harm civilian populations and that food might be a vehicle for disseminating such agents [130].

We have a lot of various specialized agencies and international organizations dealing with bioterrorism issues directly or indirectly, beginning from prevalence public health policy, intelligence or secret service, law enforcement and public health bodies, finally to agencies responsible for resilience and return to the state before the event. Many of them are working on international or regional level – European Union (EU), North Atlantic Treaty Organization (NATO), Organization for Security and Co-operation in Europe (OSCE), International Committee of the Red Cross (ICRC), United Nations Interregional Crime and Justice Research Institute (UNICRI), United Nations Institute for Disarmament Research (UNIDIR), United Nations Office for Disarmament Affairs (UNODA), United Nations Security Council Resolution 1540 (UNSCR 1540) Group of Experts and provide guidelines, support or technical assistance to local and state agencies in developing coordinated preparedness plans and response protocols. They often organize conferences, workshops, trainings and provide self-assessment tools for terrorism preparedness including performance standards and/or attack simulations. In addition, they support applied research to develop innovative tools and strategies to prevent or mitigate illness and injury caused by biological terrorism.

Apart from that many NGOs like Biosecu.re, BioWeapons Prevention Project (BWPP), Center for Security Studies (CSS), Geneva Centre for Security Policy (GCSP), Geneva Disarmament Platform (GDP), Institute for Security Studies (ISS), International Office for Innovation in Reducing Crime Ltd. (IOIRC), Johns Hopkins Center for Health Security (CHS), World Anti-Bioterrorism Organization (WABO) deal with countering the threat posed by terrorist use of CBRN materials, too.

Legislation has a central role in countermeasures dedicated bioterrorism and proliferation of biological weapon. National legislature based on international agreements should (1) punish the production, stockpiling, transfer and use of bioweapons, (2) monitor the usage of biological agents and dual-use technology that lend development of bioweapons. Moreover, (3) establishment of national and international databanks that monitor transfer of biological agents and dual-use goods, their use in industry outreach programs, their licensed availability in national, regional and international markets as well as (4) establishment and use of confirmatory protocols in the destruction and dispersal of outdated stockpiles are recommended to mitigate the bioterrorism risk [131].

Additionally, BWC's Confidence-Building Measures (CBMs) sustained by use of monitoring and verification protocols contributes biosecurity measures via reducing and eliminating threats of biological warfare and bioterrorism. Also development of national guidance or setting of recommendations for biosecurity facilities working with, storing and transporting "high consequence pathogens", namely, in

clinical laboratories, hospitals, research universities, private industry or numerous state and federal facilities will be also favorable.

Finally, without domestic legislative framework, any native agency or emergency service cannot respond to or initiate investigation of any crime [132].

12.6 Conclusion

Each incident with high risk biological agents, no matter about intention, poses a real danger for human, animals, plants and ecosystems they live. Biological agents acquired from natural sources or genetic engineering labs may cause severe illnesses or deaths, unless adequate preventive measures are used. Application of biosafety measures by employees will minimalize a risks associated with biological agents in the workplace. On the other hand, an effective biological threats assessment and management using biosecurity measures may prevent or reduce probability of deliberate release.

Based on lessons learned from history several preventive strategies against terrorism using weapons of biological warfare had been developed. Due to wide scope of biosafety and biosecurity interests synchronized strategy of different institution dealing with biological agents should be discussed. One of the most important is implementation of legislative framework and adherence a rigorous policy in reference to biological safety and security. The both, legally and non-legally binding instruments on biosafety and biosecurity ought to be implemented on each governmental level – international, regional and domestic, respected and used in practice.

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