

SYNOPSIS OF BIOLOGICAL SAFETY AND SECURITY ARRANGEMENTS

Summaries of key international treaties, agreements, instruments, guidelines, multilateral engagement mechanisms, and information resources intended to guide national approaches to biosafety in research, clinical, and industrial laboratories.

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July, 2015

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Acknowledgements

This project was supported by the Naval Postgraduate School Project on Advanced Systems and Concepts for Countering WMD (PASCC) Grant No. N00244-15-1-0028 to provide funding support for research entitled "Improving Security Through International Biosafety Norms."

The authors would like to acknowledge Drs. Barbara Johnson, Jonathon Richmond, Piers Millet, Nicoletta Previsani, Ren Salerno, and Rebecca Katz for their helpful insights and sharing their wealth of knowledge to shape the synopsis. The authors would also like to acknowledge the Nuclear Threat Initiative, which had sponsored a Biological Safety Primer that was the foundation for this synopsis, and Ryan Morhard, JD, who co-authored that work.

Introduction

This Synopsis provides summaries of key international treaties, agreements, instruments, guidelines, multilateral engagement mechanisms, and information resources intended to guide national approaches to biosafety in research, clinical, and industrial laboratories. It summarizes the benefits and limitations of each in promoting biosafety, and their individual contributions towards minimizing the global risk and consequences of laboratory accidents. Though the compilation of these arrangements, we have determined that there is an extensive array of existent governmental mechanisms related to biosafety. However, this work also exposed a major gap in international biosafety coverage related to the potential for high-consequence accidents: there remains a need for international norms for the biosafety and governance of those pathogens that have increased potential to spark a pandemic.

Most accidents in biocontainment laboratories are limited to the researchers involved and possibly their close contacts. While these accidents are unfortunate events that may have severe consequences for those directly affected, these incidents would not typically become matters of international concern. However, laboratory acquired infections (LAIs) with particularly transmissible pathogens, including non-circulating human influenza strains, Severe Acute Respiratory Syndrome (SARS), or engineered influenza strains could have consequences that go well beyond the laboratory, beyond borders, and could constitute a threat to national and global security.

High-consequence pathogens work requires not only careful attention and training of the researchers performing the work, but a system of biosafety training, engineered controls, monitoring, and a safety culture. However, not all laboratories are so equipped, staffed, supported, or have the necessary oversight mechanisms in place to safely conduct this work. This synopsis of biosafety-related international agreements exposes gaps in biosafety norms for high-consequence research that may lead to accidents with pandemic potential, and which should be addressed to increase laboratory safety, worldwide.

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I. ARRANGEMENTS WHICH DIRECTLY CONCERN BIOSAFETY

WHA 58.29

Overview and Benefits

The 2005 **World Health Assembly Resolution 58.29 Enhancement of Laboratory Biosafety**, directly deals with biosafety in the 194 World Health Organization (WHO) Member States, which include all members of the United Nations except Liechtenstein.^{1,2} The Resolution acknowledges that the release of microbiological agents and toxins may have global ramifications, and aims to prevent outbreaks of emerging and re-emerging diseases such as SARS.

This Resolution acknowledges that while many Member States have effective biosafety controls and guidelines, others do not. The WHA Resolution therefore urges Member States to do the following:

- Review the safety of their laboratories and their existing protocols for the safe handling of microbiological agents and toxins, consistent with WHO's biosafety guidance;³
- Implement specific programs, consistent with WHO's biosafety guidance, to promote biosafety laboratory practices for the safe handling and transport, including containment, of microbiological agents and toxins;
- Develop national preparedness plans and national programs that enhance compliance of laboratories, including those within the government, at universities and research centers and in the private sector, particularly those handling highly virulent microbiological agents and toxins, with biosafety guidelines for laboratory practices;
- Mobilize national and international human and financial resources to improve laboratory biosafety, including containment of microbiological agents and toxins, in order to minimize the possibility of laboratory-acquired infections and resultant spread to the community;
- Cooperate with other Member States to facilitate access to laboratory biosafety equipment, including personal protective equipment and containment devices, for the prevention and control of laboratory-acquired infection;
- Encourage the development of biological-safety training programs and competency standards for laboratory workers in order to improve safety awareness and safe laboratory practices.

The Resolution requests the Director-General of WHO to ensure that WHO plays an active role to improve laboratory safety, to provide support to the generation and sharing of knowledge and experience among Member States, and to provide technical support for strengthening laboratory

biosafety. It requests regular reports to the WHA Executive Board on the implementation of the Resolution.

Limitations

- While WHA 58.29 urges Member States to adhere to principles that would increase biosafety, there is no assessment of whether the WHA guidance has been adopted by any Member State, or that sufficient funds have been committed to training, equipment, and other resources and infrastructure required in order to maintain safe and productive laboratories.
- There is no independent mechanism to monitor adherence to principles through reporting or external review, and countries do not need to report on their adherence to the resolution.
- The WHA executive board has received no reports on the implementation of the resolution, and the WHA has not addressed biosafety since this resolution in 2005.
- Member States need to request technical help to comply with 58.29 from WHO in order to receive it, but there is not an independent assessment of whether help is needed and should be requested. The WHO has provided support to strengthen biosafety in Member countries, holding six Biosafety and Biosecurity Awareness Workshops between 2005 and 2008, educating participants from more than 95 countries.⁴
- It does not provide guidance for implementing a national biosafety system, such as guidance for developing training standards, designating governmental regulations, or a system for reporting and monitoring laboratory acquired infections.
- The proportion of the need for technical assistance by the Member States exceeds WHO's capacity to provide.

International Health Regulations (2005)

Overview and Benefits

The International Health Regulations (IHR) are an international legal instrument binding all 194 Member States of the WHO. The IHR entered into force on 15 June 2007, and aims to improve the capacity of all countries to detect, assess, notify, and respond to public health threats.⁵ It requires that countries report to WHO disease outbreaks and other events that could be transnational threats—termed public health emergencies of international concern (PHEIC). There is a short list of diseases for which a single case would constitute a PHEIC, which includes smallpox, poliomyelitis, human influenza caused by new subtypes, and SARS. Other diseases and public health events are determined to be a PHEIC through a national-level assessment that determines whether it should be categorized as a transnational threat. In some nations, potential PHEICS are evaluated by WHO to assess the ability of the event to spread across borders and its public health impact, and in others, this assessment is performed by a designated national committee.

There are 8 core capacities which countries are expected to meet “to detect, assess, notify, and report events.” These include national legislation, coordination, surveillance, response, preparedness, risk communication, and human resources. The 8th core capacity is Laboratory Capacity. These core capacities are mandatory for all countries. Laboratory biosafety and biosecurity practices must also be reported to the WHA every year.

State Parties need to establish mechanisms for providing “reliable and timely laboratory identification of infectious agents and other hazards likely to cause public health emergencies of national and international concern, including shipment of specimens to the appropriate laboratories if necessary.”⁶ The total capacity scores are calculated by regions based upon whether the country has achieved a number of capacities for laboratory services. A number of those capacities relate to biosafety: biosafety guidelines accessible to laboratories; a responsible entity designated for laboratory biosafety and security; staff trained in laboratory biosafety and biosecurity guidelines; an institution responsible for inspection for compliance with biosafety requirements identified; and whether the nation has laboratory biorisk assessments conducted to update their biosafety regulations.

Limitations

- The purpose of the IHR is to detect and respond to disease threats, and laboratory services are an integral part of that mission. However, the laboratories that are part of the IHR assessment are primarily medical and public health laboratories which would be used in the course of surveillance and diagnosis of disease. Research, industrial, and commercial laboratories (both the capacity level and activities within those laboratories) are not explicitly covered under IHR obligations.
- At the policymaker level, the import of the IHR is that each State Party has obligations to prevent and control the spread of disease inside and outside its borders, and to report

potential public health emergencies of international concern to WHO. Biosafety is of incidental importance to the IHR and is not mentioned in the IHR “Guidance for National Policy-makers” which is distributed by the World Health Organization.⁷

- Laboratory capacities may not have been met: Despite the requirement for WHO Member States to have established IHR core capacities by 2012, over 80% of countries have either requested an extension or have not reported on these critical capacities, so laboratory capacities are currently unknown.⁸
- The IHR relies on self-reporting and assessment by nations, so there is no independent mechanism to monitor commitments or provide assurances to other countries through reporting or external review.
- The IHR does not provide guidance for implementing a national biosafety system, such as guidance for developing training standards, designating governmental regulations, or a system for reporting and monitoring laboratory acquired infections.

Global Health Security Agenda (GHSA)

Overview and Benefits

In response to the poor implementation rates of the IHR 2005 standards, the United States put forth the GHSA in February of 2014 along with 30 countries, international organizations, nongovernmental organizations, and public and private entities to “accelerate progress toward a world safe and secure from infectious disease threats”.⁹ The US-led agenda is a 5-year commitment to coordinate international efforts in order to generate the political will necessary to strengthen the IHR core capacities. The IHR standards were designed to create a globally linked system to respond to infectious disease. Yet necessary resources have not been generated to implement these standards. The agenda intends to create this capital in order to complement and unite existing efforts, building off of the goals of the Biological Weapons Convention, the WHO codes, the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, and others. As of January, 2015, there are 44 countries which have become part of the GHSA.

The GHSA contains nine objectives to prevent avoidable epidemics, detect threats early, and respond rapidly and effectively to biological threats of international concern. The second objective is promoting national biosafety and biosecurity systems. This includes the following:

- Develop, implement, and sustain a national oversight program for pathogen biosafety and biosecurity that will incorporate biological risk evaluations of the nation’s biological entities;
- Develop, modernize, enact, and sustain country-specific legislation to support a national program;
- Establish a new (or mandate an existing) government agency to administer and enforce biosafety and biosecurity oversight systems; and
- Integrate field investigation and emergency response capability as an important part of the national program.

Benefits of the GHSA are its defined benchmarks to guide programs and measure success. This is in contrast to the broad terms outlined in the IHR and may assist in developing those standards that thus far have been difficult to implement. Additionally important are stratified goals for the short-term; for example, establishing emergency operation centers (EOCs) and strengthening laboratory security in 10 partner countries in 2014, and long term; setting up public and private partnerships in partner countries to ensure annual investments and sustainability of health security.

Limitations

- The GHSA is focused on giving a helping hand to more resource-constrained countries. The biosafety issues associated with gain of function and areas of research are not just in such countries—in fact, the appropriate target may be the research centers in well-resourced countries.

- The GHSA has not concentrated leadership responsibilities in the US, so it will not be as tied to US administrative shifts. Still, there is a need to be cautious and to shore up support for the initiative after 2016. A predecessor to the GHSA, the Global Health Initiative, was a six-year commitment to shifting the structure of health policy, which was announced by President Obama in 2009. However, the GHI office in the State Department closed only three years later, in July of 2012, amidst infighting and leadership questions.¹⁰
- In FY2015, the CDC is estimated to devote \$55 million to implement GHSA objectives under the Global Public Health Protection program, a decrease of \$7 million from FY2014. FY2016 budget requests \$77 million. Compared to the \$8.1 billion proposed for other global health initiatives like PEPFAR, the funding appears insufficient to achieve the GHSA's goals. However, \$5.5 billion was appropriated for the response to the Ebola outbreak in West Africa in 2 emergency appropriations, PL113-164 and PL 113-235. Of that amount, \$1.8 billion was for CDC and \$50 million for the Defense Threat Reduction Agency (DTRA).^{11,12}

CEN Workshop Agreement on Laboratory Biorisk Management (CWA 15793)

Overview and Benefits

In February of 2008, a CEN workshop agreement (CWA 15793) was published on laboratory biorisk management. CEN is the European Committee for Standardization (Comité Européen de Normalisation). CEN Workshops offer a mechanism where stakeholders in diverse areas can develop consensus standards and requirements in an open process. CEN Workshop Agreements (CWAs) can be applied to international stakeholders, but they do not have the force of regulation and conformity is voluntary. This particular CWA was developed with expert participants from 24 countries, including Argentina, Australia, Belgium, Canada, China, Denmark, Germany, Ghana, the UK, The US, and others, and it was updated in 2011.

The Laboratory Biorisk Management CWA is based upon a management system approach and on the concept of continual improvement in what is known as the PDCA (Plan-Do-Check-Act) principle, to incorporate a cycle of planning, implementing, monitoring, and reviewing laboratory management. The goal of the agreement is to set requirements necessary to control risks associated with the handling or storage and disposal of biological agents and toxins in laboratories and facilities.

The CWA is targeted to organizations that are in need of maintaining a biorisk management system, and sets out performance based requirements so that those organizations can demonstrate that appropriate and validated risk reduction procedures have been established and implemented. For example, one of the requirements is for organizations to have a biorisk management committee, which would have a representative cross section of expertise, would ensure that issues are formally recorded, and which would meet at a defined and appropriate frequency. For US research organizations, this requirement is often fulfilled by an “Institutional Biosafety Committee.” There are many other practitioner-level topics covered in the CWA, including risk assessment, pathogens and toxins inventory and information, personnel and competency, good microbiological technique, clothing and personal protective equipment (PPE), facility physical requirements, equipment and maintenance, decontamination and others.

Research organizations, medical laboratories, and industries within all of those countries as well as other countries may find it useful to adopt the provisions in this CWA as it could provide their organization with a “Good Housekeeping seal of approval,” but the agreement does not automatically apply to the countries which had participants in its development. In 2011, the agreement was extended without revision for 3 years, and it is due to expire in 2014. Providing CEN approval in December 2014, the current trajectory is for the CWA 15793 document to be transferred to the International Organization for Standardization (ISO) and adapted into a deliverable for accreditation.¹³

Limitations

- There is no independent assessment of an organization’s voluntary adherence to the standard.

- This agreement is aimed at practitioners so that their research organizations or industrial laboratories may achieve this standard. It is not a national policy-level standard. It does not provide guidance for implementing a national biosafety system, such as guidance for developing training standards, designating governmental regulations, or a system for reporting and monitoring laboratory acquired infections.
- Due to its origins in the European workshop agreement framework, there is a great deal of confusion amongst practitioners in countries outside Europe, including in the US, about whether this CWA is applicable outside Europe.
- It is not known how many laboratories and organizations adhere to this standard. EBSA performed a voluntary survey of 114 biosafety professionals in Europe in preparation to transfer the CWA into an ISO International Survey. The numbers were disappointing: although 62.8% of respondents were familiar with the guidelines, only 33.3% of the professionals had the CWA 15793 implemented in their institution. However, many did state that even if it is not formally adopted, it is used for guidance and as a reference document.¹⁴
- The agreement is still used, but officially expired in 2014.

WHO Biosafety Guidance

Overview and Benefits

The World Health Organization has provided biosafety guidance for member nations since 1983, and is now operating with its 3rd edition of the Laboratory Biosafety Manual, which is freely available on its website.³ The manual provides practical guidance on biosafety for research and health laboratories, and covers such issues as risk assessment, rDNA, and guidance to commission and certify laboratories. Versions of the manual are available in English, French, Spanish, Portuguese, Chinese, Russian, Italian, Japanese, Swedish, and Vietnamese.

The manual provides information that the research or health laboratory practitioner would need in order to be safe in the laboratory. There is information about the different levels of containment laboratories (Biosafety levels 1-4), different types of biological safety cabinets, good microbiological techniques, and how to disinfect and sterilize equipment. The necessary triple packaging required to adhere to international transport regulations is described, as are other types of safety procedures that must be in place in addition to biosafety—for chemical, electrical, ionizing radiation, and fire hazards. The manual also describes the way that the research organization should be organized to continue to monitor and improve the safety in the organization, with a biosafety officer and biosafety committee.

The WHO Laboratory Safety Manual is not the only guidance document that is used worldwide. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition, which is produced by the US Centers for Disease Control and Prevention and the National Institutes of Health, is used in laboratories all over the world.¹⁵ It also offers biosafety guidance and also describes some of the regulatory requirements that US laboratory workers should be aware of, such as rDNA guidelines and select agent regulations.

Limitations

- There is no mechanism to provide assurances that the WHO biosafety guidance is being adhered to, or that people working in laboratories (medical, public health, research, or industrial) are sufficiently trained.
- It does not provide guidance for implementing a national biosafety system, such as guidance for developing training standards, designating governmental regulations, or a system for reporting and monitoring laboratory acquired infections.
- This guidance is aimed at the practitioner level, and is full of pragmatic information that could improve the biosafety of a research organization, but does not target policymakers for specific improvements to nation-wide biosafety measures.

The Cartagena Protocol on Biosafety (CPB)

Overview and Benefits

The Cartagena Protocol on Biosafety (CPB) is a binding international agreement ratified into the Convention on Biological Diversity on 11 September 2003.¹⁶ This Protocol, which applies to the 168 Member Countries, provides an international regulatory framework to ensure “an adequate level of protection in the field of the safe transfer, handling, and use of living modified organisms (LMOs) resulting from modern biotechnology.” However, the protocol is controversial; many of the leading LMO-exporting countries, like the United States and Canada, are not members. All LMOs, defined as organisms that possess a novel combination of genetic material obtained through the use of modern biotechnology, are contained under the CPB. Yet the regulations primarily address the safe transfer, handling, and use of those that may have adverse effects on the conservation of biological diversity.

There are two main principles of the CPB; 1) Advanced Informed Agreement (AIA) that allows the importer to analyze risk and determine whether or not to approve transfer, and 2) the Precautionary Principle, which allows countries to block import even without sufficient scientific evidence of potential danger.

The CPB establishes a comprehensive and transparent regulatory framework and legal obligations to assess and manage the risks of LMOs, including emergency procedures for unintentional release. Benefits of the framework include its guidance on how to evaluate and compare risks among LMOs. Specifically, the Protocol sets out principles and methodologies on how to conduct a risk assessments, establishes an expert group on Risk Assessment and Risk Management to prepare a roadmap and action plan, and organizes regional workshops on capacity-building for risk assessment and risk management. In addition, the language can easily be applied towards national biosafety regulations to inform exporters and importers of their rights and obligations. It does require each member country to enact its own national regulations to allow for implementation; however this has been a positive driving force behind countries establishing regulatory systems.

Limitations

- While the CPB does cover all LMOs, except those that are pharmaceuticals for humans already addressed by other international organizations or agreements, it does not put forth any regulations for transfer of those to be used in lab settings.
- The legislation provides a framework for assessing risk of LMOs but does not set an international standard for appropriate risk levels, thereby allowing each individual country to determine their own standards for import.
- Risk assessment does not encompass potential risks of consumption by humans or animals. Instead the Protocol is focused more on ensuring LMOs do not negatively affect biodiversity, or the degree of variation in life, such as by invading, replacing native species, or taking over the environment.

- The socio-economic aspect of the CPB is controversial and is seen as an anti-technology platform.¹⁷ The debate highlights the long-standing trade conflict between the United States and Canada against the European Union and its genetically modified organisms (GMO)-import restrictions. The United States, which has not ratified the CPB, does not consider the socio-economic impact of LMO/GMOs during the regulatory decision-making process.

OIE Biological Threat Reduction Strategy

Overview and Benefits

The World Organisation for Animal Health (OIE) is an intergovernmental organization responsible for standard-setting related to animal health for its 178 Member Countries. In January of 2012 the OIE developed a Biological Threat Reduction Strategy, which is supported by its Fifth Strategic Plan that guides the work program until 2015.¹⁸ The goal of the OIE is to create “a world that is safe and secure from accidental or deliberate release of animal pathogens, including zoonoses.”

Animal diseases are a serious threat for public health. In addition to the zoonotic diseases, pathogens that threaten livestock compromise food security and have the potential for large economic impact. There has also been a long history of using animal disease agents as bioweapons. The OIE Biological Threat Reduction Strategy develops the means for early detection and response of animal pathogens, which include a number of areas related to biosafety. Additionally steps are laid out for determining the origin of animal disease outbreak – whether it is natural, deliberate, or accidental.

There are 5 strategic areas, including the following:

1. Policies, advocacy and communication: Reduce biological risks linked to veterinary laboratories and animal facilities with efficient biosecurity and biosafety practices.
2. Maintain expertise and setting standards, guidelines, and recommendations: Develop and maintain global networks of technical expertise encompassing biosafety and biosecurity, bioethics, and biotechnology. Information from these networks also provides early warning of potential dual use technologies. Risk-based guidelines for biosafety are included in Manual of Diagnostic Tests and Vaccines for Terrestrial Animals Chapter 1.1.2 (2011).¹⁹
3. International cooperation: Cooperate with public health partners (WHO) to develop joint risk-based guidance on laboratory biosafety and biosecurity and sample shipment, also accounting for risks posed to animal health and the environment.
4. Global disease intelligence: All member countries report disease events directly online through the World Animal Health Information System (WAHIS).
5. Capacity-building and solidarity: Maintain up-to-date international standards and guidelines on disease surveillance and notification, and disease prevention and control by OIE Member Countries as well as on animal production and food safety. Member Countries are evaluated by the OIE-Performance of Veterinary Services (PVS) tool, which contains 40 core competencies to improve compliance with OIE standards.

Limitations

- As of September 2014, 120 PVS Evaluations had been completed out of the 130 requested. This does not encompass all Member Countries. Each member country has the option whether it wants to waive the confidentiality of the report. Only 86 out of the 120 have done so. Without complete transparency it is difficult to evaluate the compliance to the standards.
- The OIE is not an enforcement body. It relies on an honor system of conduct to its codes and principles based on voluntary compliance by its Members. Countries do not always comply with international standards when they establish zoosanitary requirements and tend to have inconsistent interpretations of the codes.

II. ARRANGEMENTS IN WHICH BIOSAFETY IS AN INFERRED COMPONENT

The Biological Weapons Convention

Overview and Benefits

The Convention on the Prohibition of the Development, Production, and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, more commonly known as the Biological Weapons Convention (BWC), entered into force in March, 1975, as the first multilateral disarmament treaty to ban the production and use of an entire category of weapons.²⁰ The BWC went much further in controlling biological weapons proliferation than the Geneva Protocol of 1925, because although the Protocol prohibited the use of a bacteriological weapon in war, several nations reserved the right to respond in kind if attacked.²¹ Currently, the BWC has 172 States Parties and 9 that have signed but not ratified the treaty. There are 15 states which have neither signed nor ratified the Convention.

As part of the BWC obligations, States Parties participate in a voluntary exchange of Confidence-Building Measures (CBMs), including giving information about their research centers and laboratories, biodefense research, information on outbreaks of infectious diseases, and make declarations about their national legislation and regulations that affect legitimate biological research.²² States Parties are assisted by an Implementation Support Unit (ISU).

Promoting biosafety in legitimate research is not the purpose of the BWC. Biosafety has been seen as an important treaty component for legitimate biological research activities. Evidence of that includes the State Parties' issuing of shared statements about preventing unauthorized access to pathogens, safe handling of pathogens to protect people and the environment, and the importance of biosafety training.²³ In the most recent (Seventh) Review Conference, States Parties agreed on the value of implementing voluntary management standards for biosafety and biosecurity, as well as encouraging the promotion of awareness in the life sciences community of researchers' obligations under their nation's laws, the BWC, and promoting a culture of responsibility in the life sciences.²⁴

Article X of the BWC calls for the "fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes." In the Seventh Review Conference, the Conference called upon States Parties to continue implementing Article X by strengthening existing international organizations and networks working on infectious diseases, including the WHO, FAO, OIE and IPPC; to improve communication on disease surveillance; and to improve national and regional capabilities to survey, detect, diagnose and combat infectious diseases.

Limitations

- Ensuring biosafety is not the purpose of the BWC. The BWC is primarily concerned with the misuse of biological research for purposes of creating or using a biological weapon.
- CBMs are not legally binding, but all parties have agreed to submit them. However, the vast majority of States Parties have consistently failed to submit declarations, including about their national legislation and regulations that affect legitimate biological research.
- The BWC is not universal. Non-member States are: Angola, Chad, Comoros, Djibouti, Eritrea, Guinea, Israel, Kiribati, Micronesia, Namibia, Niue, Samoa, South Sudan, and Tuvalu.
- The Implementation Support Unit, which supports countries to submit CBMs and comply with the treaty, is widely perceived to be understaffed and underfunded for their mission. The unit is made up of only three staff members.²⁵

The G8 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction

Overview and Benefits

The G8 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction (Global Partnership) began at the 2002 Kananaskis G8 Summit as a 10-year, \$20 billion initiative to prevent terrorists or states that support them from acquiring or developing WMDs.²⁶ Since then, the GP has grown to include 27 partner countries and has allocated about \$21 billion worldwide. At the 2011 G8 Summit in Deauville, it was agreed to extend the Partnership beyond 2012.

As part of the G8 Global Partnership, there is a Biological Security Sub-Working Group (BSWG) which promotes efforts to reduce risks associated with biological threats, regardless of cause, through collaboration with other member nations, International Organizations, and health and science sector counterparts. Under the BSWG, Global Partnership agreed to the following five major activities to be reviewed annually for the next five years, beginning in 2012:

1. Secure and account for materials that represent biological proliferation risks.
2. Develop and maintain appropriate and effective measures to prevent, prepare for, and respond to the deliberate misuse of biological agents.
3. Strengthen national and global networks to rapidly identify, confirm, and respond to biological attacks.
4. Reinforce and strengthen biological nonproliferation principles, practices, and instruments.
5. Reduce proliferation risks through the advancement and promotion of safe and responsible conduct in the biological sciences.

Biosafety is implicit in several of these goals, including the security and accounting of biological materials; the promotion of safe and responsible conduct, and the adoption by nations of a system of biorisk management. The presidency of the G8 rotates annually; the UK led the working group in 2013.

Progress included identifying gaps in biosecurity capacities and capabilities and securing over \$40 million for projects in the upcoming years.²⁷ The presidency was transferred to the Russian Federation in 2014. However, following Russia's annexation of Crimea, the leaders of the G-7 met during the Nuclear Security Summit in The Hague, Netherlands on March 24 and decided to oust Russia from the Group of 8.²⁸ Sanctions continue to follow. Germany took over the G7 presidency on July 1 2014, and held its first of three meetings of the Working Group of the Global Partnership against the Spread of Weapons of and Materials of Mass Destruction on November 4, 2014. The main focuses of this meeting were the Ebola epidemic in West Africa, and the need for promoting chemical, biological, radiological, and nuclear security in Ukraine. The last meeting took place in Munich at the end of April 2015.²⁹

Limitations

- The G8 GP is not directly focused on biosafety in legitimate research activities, though biosafety is implicit in their biosecurity goals.
- Commitments are non-binding.
- There is no mechanism to assess or enforce commitments or provide assurances to other countries through either mandatory reporting or external review.

Sequencing Screening Agreements

Overview and Benefits

Two sequence screening agreements have been developed by two different private sector consortia to diminish the potential to misuse commercially obtained synthesized genomic material. Though not governmental, these agreements aim to block an illegitimate or unauthorized person from ordering the synthesis of a pathogenic genomic sequence, including the select agents that are regulated in the US. There is US guidance for genomic synthesis companies operating in the US, but these 2 agreements go beyond the US minimum efforts to screen sequences and customers.³⁰

The groups that harmonize their sequence screening efforts in order to prevent misuse are the following: the International Gene Synthesis Consortium, which consists of Blue Heron, GenScript, DNA 2.0, Integrated DNA Technologies, and Life Technologies, which collectively represent 80% of gene synthesis companies worldwide, and the International Association Synthetic Biology, which includes Yagiz Alp Aksoy, Macquarie University, Australia; ATG:Biosynthetics GmbH, Germany; Biomax Informatics AG, Germany; Entelechon GmbH, Germany; Eurofins MWG, Germany; Markus Fischer, Entelechon GmbH, Germany; ICLS, USA; Peer Stähler, Germany; and Sloning BioTechnology GmbH, Germany.^{31,32} There are current efforts, led by the International Council of the Life Sciences, to expand the reach of sequence screening to additional companies that perform gene synthesis, particularly in Asia.

Limitations

- These agreements primarily address security versus biosafety, though a researcher who does not have the laboratory facilities to safely handle dangerous pathogens may be prevented from ordering one, deliberately or inadvertently. However, these agreements do not extend to authorized or normal research practice with communicable agents.
- The agreements do not yet cover all commercial gene synthesis, and would not affect gene synthesis that is not ordered commercially.
- These agreements only relate to the acquisition of the genetic material. They do not provide guidance or rules related to the safe handling of genetic material or pathogens once inside a laboratory.

WHO Smallpox Agreement

Overview and Benefits

The World Health Assembly agreed in 1999 that “outcome oriented and time-limited” experiments with live variola virus (smallpox) could be allowed at the two locations in the world where smallpox is stored: the Centers for Disease Control and Prevention in Atlanta, Georgia, and the Russian State Centre for Research on Virology and Biotechnology which is also known as VECTOR in Koltsovo, Novosibirsk Region, Russian Federation. The WHO created a scientific oversight body, the WHO Advisory Committee on Variola Virus Research, which determines the need for proposed research and reviews and approves all experiments with smallpox.³³ The committee meets every year in the fall. During the fifteenth meeting, held September 24-25, 2013 discussion focused on the destruction of the variola virus stocks.³⁴ Majority view was that there was no need to retain live variola virus beyond those studies already approved. (CDC currently has a “use to completion” protocol for 70 of its 420 variola virus stocks). This recommendation was submitted to the Sixty-seventh World Health Assembly which was held in May 2014, yet the group again postponed ruling on whether or not to destroy the stocks.³⁵ The United States is opposed to immediate virus destruction.

The WHO Recommendations Concerning the Distribution, Handling and Synthesis of Variola Virus of May, 2008, apply to scientists wishing to obtain, handle, or synthesize variola virus DNA. Membership on the Committee is inclusive of all WHO regions and the Committee is advised by at least 10 scientific experts.

Scientists who wish to obtain parts of the (non-infectious) variola virus genome for research on diagnostics or treatment of smallpox, or vaccines against smallpox can obtain DNA from either of the two WHO Collaborating Centers, but those laboratories need to formally request the DNA, agree not to distribute the DNA to unauthorized third parties, and must report to WHO annually on the status of the variola virus DNA. When handling the variola virus DNA, laboratories must be preceded by a written risk assessment in accordance with locally agreed national guidelines.

Limitations

- This agreement is limited to smallpox, which is unique among communicable diseases in that it is eradicated, held only in 2 laboratories in the world, and which has had its laboratory extinction agreed upon internationally. Final destruction of the laboratory smallpox virus stocks has been postponed pending the completion of research projects as permitted by the WHO Advisory Committee on Variola Virus Research, and with the consent of the World Health Assembly.
- This agreement provides no guidance regarding biosafety for other agents.
- The *de novo* synthesis of the smallpox virus is now possible in some sophisticated laboratories around the world—sequence information is readily available online. This capacity will become increasingly available over time.

International Air Transport Association Dangerous Goods Regulations

Overview and Benefits

The International Air Transport Association (IATA), a trade association of airlines, represents more than 240 airlines. They formulate industry policy on a range of aviation issues, and their regulations are followed by 84% of total air traffic.

IATA guidelines for the transport of dangerous goods by air, including infectious substances and patient specimens, are published in the UN Recommendation on the Transport of Dangerous Goods. They were developed in coordination with input from experts from the WHO and other technical experts in the field of transport, packaging, and health.

Specifically, the Dangerous Goods Regulations define and classify infectious substances and applicable packaging provisions and prohibitions, as well as relevant training and emergency response requirements. Infectious substances are classified as either Category A or Category B. Any infectious substance that is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, life-threatening or fatal disease (e.g. *Bacillus anthracis*) is classified as Category A and requires special packaging, marking, labeling, and documentation. Substances that do not meet Category A criteria are regulated according to Category B transport requirements.

Limitations:

- IATA regulations concern transport by air, and do not concern activities prior to packing for shipment.
- IATA regulations do not concern transport of infectious substances by other forms of transportation.

III. ARRANGEMENTS WHICH DO NOT HAVE A BIOSAFETY COMPONENT, BUT WHICH ARE BIO/BIOSECURITY RELATED

UN Security Council Resolution 1540

Overview and Benefits

The United Nations Security Council Resolution 1540 (UNSCR 1540), which was issued in 2004, calls for all UN Member States to develop and enforce their own legal and regulatory measures against the proliferation of chemical, biological, radiological, and nuclear weapons and their means of delivery, in order to prevent the spread of weapons of mass destruction to non-state actors.³⁶ The resolution was prompted in large part after it was revealed in 2004 that a Pakistani nuclear scientist, known as A.Q. Khan, had transferred technology and knowledge to North Korea, Iran, and Libya.³⁷

UNSCR 1540 complements the Biological Weapons Convention because it requires all UN Member States to comply whether or not they are States Parties to the BWC. UNSCR 1540 requires States to adopt and enforce appropriate laws to prohibit non-state actors to manufacture, acquire, possess, develop, transport, transfer or use nuclear, chemical or biological weapons and their means of delivery, in particular for terrorist purposes. States must also not participate in those activities as an accomplice, assist or finance them. States are called on to work with and inform industry and the public regarding their obligations.

The 1540 Committee is supported by up to 8 national experts and the UN Secretariat Office for Disarmament Affairs and Department of Political Affairs. The Committee is responsible for managing the implementation of Resolution 1540. States are required to report progress towards implementation to the committee, which had its mandate extended in 2011 until 2021. In addition to drawing on expertise from civic society and the private sector, the 1540 Committee facilitates assistance and capacity-building by matching offers and requests for assistance between states (e.g. through visits to States, at the invitation of the State concerned, assistance templates, and action plans).

Limitations

- UNSCR 1540 does not explicitly address biosafety.
- UNSCR 1540 does not concern naturally occurring pathogens or sources, such as hospitals, medical waste, and diagnostic labs, nor does it concern legitimate research laboratories.

The Australia Group

Overview and Benefits

The Australia Group is an informal, voluntary export-control harmonization agreement consisting of 42 nations and the European Commission.³⁸ It was originally established in 1985, soon after the use of chemical weapons in the Iran-Iraq war. Australia Group nations coordinate their nation's export control lists for equipment, chemicals, biological agents, and related technologies and knowledge to reduce proliferation of chemical and biological weapons. The Group accepts new members only by consensus. All Australia Group members are also States Parties to both the Biological Weapons Convention (BWC) and Chemical Weapons Convention (CWC).

The Australia Group meets every year in Paris to coordinate export control lists and policies, discuss revisions, and share intelligence about export denials. For biological agents and related items, prohibited exports include such biological agents as smallpox, Marburg virus, foot and mouth disease, and *Bacillus anthracis*, the causative agent of anthrax disease, and dozens of others—in all, there are 80 biological viruses, bacteria, toxins, and fungi on the list of controlled biological agents for which Group members are expected to have export control procedures.³⁹ In addition, there is a list of controlled dual-use biological equipment which could be used for both legitimate research and BW development, which include fermenters, complete biological containment facilities, freeze drying equipment, and aerosol testing chambers.⁴⁰

Limitations

- The Australia Group focuses on weapons proliferation, and does not address the safety and handling of biological pathogens for legitimate purposes by either member or nonmember nations.
- The Australia Group is not universal. Russia, India, and China are not member states but do possess national export controls for some, but not all, of the items on the list.⁴¹

Proliferation Security Initiative (PSI)

Overview and Benefits

The Proliferation Security Initiative (PSI) is an informal grouping of states which have joined together to prevent trafficking by detecting and intercepting weapons of mass destruction, WMD-related materials, and means of delivering WMDs.⁴² PSI was launched in 2003, soon after 15 Scud missiles were found on board an unflagged North Korean freighter headed towards Yemen, but that intercepted shipment was determined to be legal according to international law, and thus released. There are 103 nations which support the initiative, but *non*-endorsers include India, China, and Indonesia.⁴³

The PSI Statement of Interdiction Principles commits participants to establish a more coordinated and effective basis through which to impede and stop items that contribute to proliferation of WMD.

Countries commit to:

- Interdict transfers to and from states and non-state actors of proliferation concern to the extent of their capabilities and legal authority.
- Develop procedures to facilitate the exchange of WMD information with other countries.
- Strengthen national legal authorities to facilitate interdiction.
- Take specific actions in support of interdiction efforts.

Limitations

- The focus of PSI's efforts to date has been entirely on nuclear and chemical security, not biological, and there are no public plans to emphasize biological issues.
- PSI focuses on weapons trafficking, and does not address the safety and handling of biological pathogens for legitimate purposes by nations, groups, or individuals.
- Participation is voluntary.
- Commitments are non-binding.
- Participation is not universal.
- Boarding agreements apply only to commercial transportation, not government transportation.

IV. ASSOCIATIONS THAT ADDRESS BIOSAFETY

Overview and Benefits

There are numerous associations that have been formed over the last 15-30 years that are dedicated towards improving biosafety. These groups tend to become centers for experts to disseminate information broadly across regions or internationally and assist in communicating best practices. They advocate at international meetings and during the development of the aforementioned arrangements on behalf of scientists in order to influence and support the generation of international legislation. In addition, these associations help to implement the biosafety regulations through capacity building.

Groups include:

- Regional or International non-profit associations:
 - **European Biosafety Association (EBSA)** – regionally focused on defining tasks and skills for biosafety professionals under the CEN agreement.
 - **International Society for Biosafety Research (ISBR)** –developing best biosafety practices for science performed on living modified and genetically modified technologies
 - **American Biological Safety Association (ABSA)** – regionally focused on providing a forum for exchange of biosafety information and to serve the biosafety needs of professionals.
 - **Asia-Pacific Biosafety Association (A-PBSA)** – regionally focused on advanced safety and security knowledge and sustainable practices.
 - **African Biological Safety Association (AfBSA)** – regionally focused on enhancing knowledge and practices of biosafety and biosecurity primarily in central Africa.
 - **International Federation of Biosafety Associations (IFBA)**; previously International Biosafety Working Group (IBWG) was established in 2001. This is the overarching group, containing representatives from the International Veterinary Biosafety Working Group (IVBWG), WHO, EBSA, ABSA, and the A-PBSA. They hold biannual meetings and developed and publicized the International Compendium of Regulations, Guidelines and Information Sources.⁴⁴ Recently, the IFBA launched an international certification program for biosafety professionals.
- Government programs aiming to bring biosafety to other countries
 - **Cooperative Biological Engagement Program (CBEP)** – arm of the Defense Threat Reduction Agency (DTRA) that works to assist partner nation governments in addressing the obligations of the UN National Security Council Resolution 1540 (page 13) and to enhance partner countries’ capacities to detect and respond to public health emergencies.
 - **Biosecurity Engagement Program (BEP)** – arm of the Department of State that engages life scientists to combat international biological threats by building sustainable capacity for biosecurity and biosafety.
 - **Sandia National Laboratories** – part of the Department of Energy, developed two biorisk assessment models for use at laboratories to identify and improve upon risk measures.⁴⁵

- Select non-governmental associations that work towards biosafety (not an exhaustive list)
 - **CRDF Global:** promotes international scientific and technical collaboration through grants, technical resources, training and services.
 - **Griffin Institute** – working globally to develop and deliver biorisk management solutions. Provides support for ABSA research grants and events like the annual Leadership Institute for Biosafety Professionals.
 - **Verification Research, Training and Information Centre (VERTIC)** – promotes effective verification of international agreements as they are concerned with arms control and disarmament.
 - **International Council for the Life Sciences (ICLS)** – operates internationally to enhance global biological security. Notable achievements include assisting in the creation of the Biosafety and Biosecurity International Consortium (BBIC), bringing biosafety strategies and associations to the Middle East and North Africa (MENA) region

Limitations:

- There is an abundance of working groups that deal with biosafety. Many functions overlap. There is an opportunity to define roles in a way that has yet to be done in order to ensure effectiveness of all.

V. ENDNOTES

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