NTI:bio

Preventing Global Catastrophic Biological Risks

Lessons and Recommendations from a Tabletop Exercise Held at the 2020 Munich Security Conference

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Open Philanthropy Project

This tabletop exercise was held under Chatham House Rule. Quotes from the tabletop exercise participants are included throughout the report but remain unattributed in keeping with this rule.

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Foreword

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The COVID-19 pandemic has infected millions, left one million dead, shattered global economies, and exposed governments and international organization as ill-prepared and ill-equipped to manage the kind of catastrophic biological event that public health and global security officials have warned of for years. In our interconnected world, biological threats are only increasing. The risk landscape is also changing, with recent technology advances enabling easier, cheaper, and faster tools to produce and modify pandemic agents that could pose an even greater threat to humanity.

In mid-February 2020, during the Munich Security Conference, and just after the World Health Organization declared COVID-19 to be a Public Health Emergency of International Concern, the Nuclear Threat Initiative (NTI) convened senior leaders from around the world for a scenario-based exercise focused on high-consequence biological threats. Although the event had been planned for months, the fictional disease in the scenario swept the globe in a way eerily similar to COVID-19 and foreshadowed the widespread impact and paralyzing knock-on effects that the world is now experiencing. While the real-life novel agent—SARS-CoV-2—emerged from nature, the next pandemic threat could be caused by a laboratory accident or deliberate misuse, arising at any time.

A key goal of NTI's exercise in Munich was to identify the most effective approaches for preventing and responding to globally catastrophic biological events. The meeting highlighted the need for trusted and non-politicized mechanisms for scientists and public health experts to collaborate during a biological crisis, rapidly identify the responsible pathogen, and discern its origin. Allegations about the source of the COVID-19 pandemic have demonstrated that the world needs an internationally credible, swift, transparent, and science-based approach for promptly investigating these issues. In its absence, fear, mistrust, and lack of clarity are inevitable—as we have observed in recent months. To avoid these pitfalls for the long term, it is also vital to build a more robust underlying system for maintaining transparency and building confidence among nations about bioscience research and development. Ongoing transparency efforts are critical for reducing the risk of dangerous misperceptions and suspicions about the capabilities and intentions of national governments.

In addition, we must also remain cognizant of other emerging risks already at our doorstep. A future high-consequence biological event could be caused by the accidental or deliberate release of a synthesized or engineered biological agent. Developing biotechnologies have an inherent dichotomy: they are essential for reducing pandemic threats and supporting sustainable development, but they also carry risks that have the potential to undermine progress toward achieving these same health and economic goals.

NTI is taking a number of steps in cooperation with key partners to address these risks:

- To help plan a future where it is possible to advance new biotechnologies while simultaneously reducing the risks associated with them, NTI is collaborating with the World Economic Forum (WEF) and experts from around the world to strengthen biosecurity measures for benchtop DNA synthesis. Benchtop DNA synthesis devices are an important new tool for biological research, but they can also be used to synthesize a wide range of pathogens, such as the 1918 pandemic influenza virus, SARS-CoV-2, or a novel virus that is more transmissible and virulent. In January at Davos, NTI and WEF jointly called for a new common global mechanism to screen DNA orders—to ensure that the building blocks of dangerous pathogens don't fall into the hands of malicious actors—and we described the potential to establish a new international entity to identify and reduce emerging biological risks to prevent biotechnology catastrophe.
- Just a few months before COVID-19 made headlines, NTI and the Johns Hopkins Center for Health Security released the Global Health Security Index, in partnership with The Economist Intelligence Unit, identifying preparedness gaps across 195 countries and calling for greater international coordination to manage prevention and response. COVID-19 has demonstrated that international capacity to address the kinds of infectious disease outbreaks that can lead to epidemics or pandemics is sorely lacking. It has also revealed insufficient financing for preparedness and a dearth of reliable regional approaches to securing the supply chain for materials essential for an effective response—including testing reagents, personal protective gear, and lifesaving medical equipment.

It is clear now that heads of state must prioritize pandemic preparedness as an international security imperative and that the United Nations should be in a stronger position to help coordinate a global response—including through the addition of a dedicated facilitator for high-consequence biological events housed within the Office of the UN Secretary-General. Global leaders also must commit to strengthening the World Health Organization, and a 2021 heads-of-state summit on biological threats could build political will, advance sustainable financing, and kick-start global action to fill gaps.

As NTI learned at the February exercise in Munich and as COVID-19 has demonstrated, the world's extreme lack of preparedness sheds light on the critical importance of national leadership and effective internationally coordinated efforts to marshal an effective response to this global crisis. We have a responsibility to take action now to reduce emerging biological risks—before the next pandemic strikes.

Executive Summary

In mid-February, during the Munich Security Conference, as news reports began to emerge that people in the Chinese city of Wuhan were becoming gravely ill as a result of the initial COVID-19 outbreak, the Nuclear Threat Initiative (NTI) convened a group of senior leaders from around the world for a scenario-based tabletop exercise on high-consequence biological threats. Similar to NTI's previous exercise, conducted during the 2019 Munich Security Conference, the event was designed to identify gaps in global capabilities to prevent and respond to a high-consequence biological event.[1]

By the summer of 2020, the whole world understood the devastating impact of a naturally occurring, rapidly spreading virus. Governments and international organizations struggled to respond to the COVID-19 pandemic as the global death toll climbed well into the hundreds of thousands, and millions of people remained out of work, with businesses shuttered and corporations going bankrupt.

In this exercise, participants were presented with a fictional scenario in which the world is confronting a disease outbreak from a dangerous, apparently human-engineered pathogen, which is suspected to have originated in a country with biotechnology development ambitions. Ultimately, an international investigation reveals that the suspect country has been conducting illicit bioweapons research, and an accidental release from one of its laboratories is the source of the outbreak, which eventually kills more than 50 million people worldwide.

Designed in the fall of 2019 in consultation with technical and policy experts, the exercise was not intended to address the emergence and spread of the COVID-19 pandemic. Instead, it was focused on two key goals: (1) highlighting emerging biological risks associated with rapid technology advances and discussing governance measures to reduce these risks; and (2) examining current and proposed new mechanisms for preventing, deterring, and responding to development of biological weapons by sophisticated actors, such as states.

The exercise also uncovered some key gaps in the international system, as well as priorities for future international collaboration

1 "NTI Tabletop Exercise for Senior Global Leaders on International Response to Deliberate Biological Events" (February 2019), available at www.nti.org/about/projects/global-biosecurity-dialogue/tabletop-exercise-senior-global-leaders-international-response-deliberate-biological-events/.

that are relevant to the ongoing COVID-19 pandemic and important for reducing the significant public health, economic, and security risks posed by potential future catastrophic biological events of any origin. In particular, the exercise was designed to highlight the growing biological risks as a function of the increasingly interconnected world, and the possibility that future pandemics—particularly those caused by engineered or synthesized biological agents—could have even more devastating consequences for human populations around the world. Participants determined that even as global leaders urgently respond to COVID-19, they must consider bold changes to the international biosecurity architecture to prevent an even graver risk to the future of humanity.

After the exercise, the organizers developed a set of recommendations based on findings from the discussion among exercise participants:

1. Reduce Biotechnology Risks and Implement Global Norms for Life Science Research

Exercise participants noted the lack of national or global norms and systems for identifying emerging biological risks associated with technology advances and for effectively reducing those risks through governance of life science research. At the most fundamental level, the international community lacks a shared perspective—or norms—about how to determine whether dual-use bioscience research and development activities should move forward and how to weigh the perceived benefits of the work against the potential safety or security risks that it poses. National governments, academia, and the private sector also lack the means to *act* on these norms; they lack clear and effective governance mechanisms to oversee dual-use bioscience work from early-stage design and funding decisions, through project implementation, and on to publication.

To address these problems, the organizers recommend:

- A United Nations (UN) agency or credible non-governmental institution should partner with experts from the scientific, philanthropic, security, and public health sectors to create an international entity dedicated to identifying and reducing emerging biological risks associated with technology advances and reducing global variations in oversight for dual-use life science research.
- Research organizations should require and provide incentives to those whom they fund to identify and reduce the risk of accidental or deliberate misuse in

the design, conduct, and sharing of life science research and biotechnology.

2. Enhance Transparency to Build Trust and Reduce Uncertainty

Participants discussed the lack of robust international transparency measures that could reduce mistrust and clarify the intentions and capabilities of bioscience and biodefense research being conducted across the globe. The exercise was designed to draw attention to the dangerous misperceptions among nations about suspected biological-weapons-related activities resulting from insufficient transparency and confidence-building measures. Political divisions and technical disagreements among national governments about the feasibility of establishing a verification regime for the Biological Weapons Convention (BWC) have continued to stymie progress on bolstering international transparency measures, and recent voluntary peer review efforts have not filled this gap. To help meet this need, participants noted that the private sector can play an important leadership role in shaping new voluntary efforts to enhance transparency for life science research and commercial applications.

To address this challenge, the organizers recommend:

- International organizations, national governments, academia, and the private sector should develop and implement a variety of enhanced transparency measures to reduce the risk of misperceptions about the capabilities and intentions of any nation's bioscience research and development activities. These measures could include written reports, scientific exchanges, site visits, and research exchanges.

"We have accepted that we cannot verify if a country is pursuing biological weapons, and that precludes constructive discussion around verification. How can we build trust and confidence? How can we cooperate and build confidence between sovereign countries without too much interference? The race between cooperation and catastrophe applies here."

— EXERCISE PARTICIPANT

3. Develop Capacity to Rapidly Investigate Biological Events of Unknown Origin

Participants highlighted the lack of an international approach for conducting investigations to determine the source of any high-consequence biological event of unknown origin. While the World Health Organization (WHO) has a mandate to lead the public health response and investigate the origin of naturally emerging infectious disease outbreaks, and the UN Secretary-General's Mechanism has the authority to investigate an alleged deliberate biological attack by a state, there is no

intermediate mechanism for investigating biological events that may fall between these two ends of the spectrum.

To bridge this gap, the organizers recommend:

- The international community should develop a Joint Assessment Mechanism to enable a multinational team to investigate the origin of a high-consequence biological event. This mechanism would address cases where there is ambiguity about the source of a biological event—specifically, whether it emerged naturally or was deliberately or accidentally released from an academic, commercial, or government laboratory.
- The Office of the UN Secretary-General should designate a permanent facilitator or unit to develop the capacity for and lead a coordinated, multi-sectoral response to high-consequence biological events of unknown origin.

Full findings and recommendations begin on page 19.

About the Exercise

The February 2020 Tabletop Exercise on High-Consequence Biological Threats—designed and conducted before the emergence of SARS-CoV-2 and the resulting COVID-19 pandemic—examined current and proposed new mechanisms for preventing, deterring, and responding to accidental or deliberate high-consequence biological events, including those associated with the development of engineered agents and/or biological weapons. Like naturally occurring diseases, these threats pose an increasing catastrophic risk to the global community and require new approaches to bolster existing, effective risk-reduction methods and to develop novel ideas that have the potential to dramatically reduce risks.

The scenario was developed in 2019 in consultation with technical and policy experts (see Appendix A). In advance of the exercise, which was conducted in Germany during the Munich Security Conference, NTI conducted a daylong exercise in Washington, DC, in December 2019 (see Appendix B for participant list). This version of the exercise included a deeper dive into deterrence and prevention of catastrophic biological risks posed by potential state-sponsored bioweapons research, to include accidental and deliberate release of biological weapons.

While the exercise in Munich was not intended to address the emergence and spread of SARS-CoV-2 or the response carried out by the international community, organizers and participants found that the exercise exposed important gaps and revealed priorities for future international collaboration that are both relevant to the ongoing pandemic and important to reducing the significant health, economic, and security risks posed by future catastrophic biological events of any origin.

PARTICIPANTS

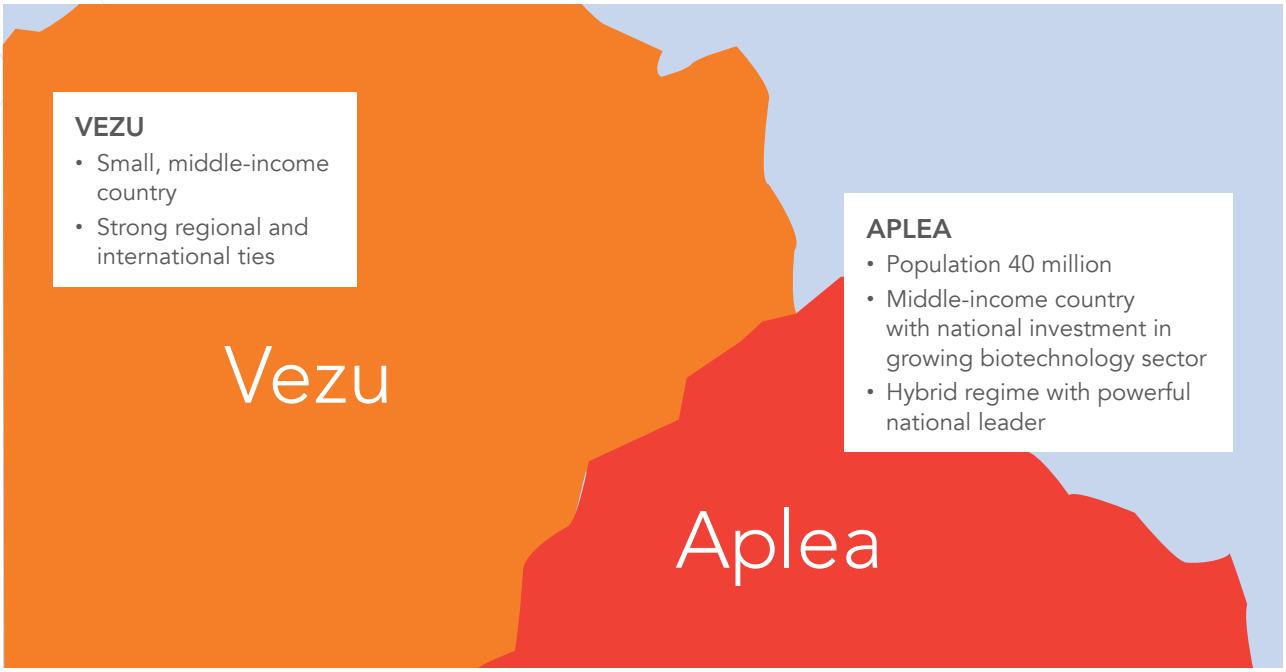
The February tabletop exercise convened an international group of current and former senior leaders with decades of combined experience leading public health responses, peacekeeping missions, and law enforcement and security investigations, and providing financing for health emergencies. Participants were asked to consider the scenario and candidly discuss gaps in mechanisms, coordination, and information sharing to reduce biological risks associated with advances in technology and high-consequence biological events. See page 11 for a complete list of participants.

"A crisis of this magnitude will make the world look different, and we wouldn't be looking back. We'd be looking forward with opportunity for change."

— EXERCISE PARTICIPANT

EXERCISE SCENARIO

The events in this fictitious scenario begin in late summer 2020 as a deadly, unexplained influenza virus kills a number of international travelers from Aplea, a middle-income



Map of the fictional country of Aplea, the epicenter of the outbreak, and neighboring Vezu.

country with a burgeoning bioscience and biotechnology economy. Research teams from two World Health Organization collaborating centers quickly sequence the responsible strain and identify it as an engineered version of H2N2 influenza, which is related to a strain that circulated among humans several decades ago. This assessment is based on the inclusion of mutations known to reduce the effectiveness of antiviral medications and the insertion of a series of changes that have previously been associated with a severe immune system overreaction, increasing the likelihood of death. Despite an emerging international consensus that this is a laboratory-created virus, the intent and identity of the creator remain unknown.

As the scenario progresses, global researchers conducting viral-strain analysis and epidemiological modeling identify a state-run laboratory in Aplea as the likely source of the outbreak, but Aplea asserts that this laboratory is part of an ongoing biopreparedness program. The scenario concludes with additional intelligence sources—including former laboratory workers—providing irrefutable evidence that the state-run laboratory in Aplea is in fact a bioweapons facility and that the spread of the deadly virus resulted from an accidental release. By the end of the exercise, the global case count is more than two billion, and more than 50 million lives have been lost as a result of the virus's spread.

The case counts and fatality counts for this exercise were based on an epidemiological model—specifically a Susceptible–Exposed–Asymptomatic–Infectious–Recovered (SEAIR) compartmental, deterministic model, which is commonly used in the public health community. In this scenario, it is assumed that the outbreak was initiated by four initial index cases in the fictional capital of Aplea and that it spread internationally over the following few weeks via passenger air flights. NTI based the pathogen epidemiological parameters on H2N2 influenza literature

February 2020 Munich Security Conference Tabletop Exercise Participants

Keynote

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Co-Chair, Global Preparedness Monitoring Board
Former Prime Minister of Norway
Former Director-General of the World Health Organization

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Dr. Adrian Thomas
Vice President, Global Public Health, Johnson & Johnson

Facilitator

Dr. Kevin P. O'Prey
Managing Partner, Palisades Group, LLC

"Technology is becoming so ubiquitous. Companies would want to know about abuse, but in the absence of regulation, it becomes challenging."

— EXERCISE PARTICIPANT

and assumed that the main public health intervention deployed by governments prior to vaccine development was case isolation. (For further information on the epidemiological model, including underlying data sources and assumptions, see Appendix C.)

QUESTIONS FOR EXPLORATION

The first goal of the exercise was to highlight the emerging biological risks associated with advances in science and technology and have participants discuss governance measures that can meaningfully reduce these risks. The second goal was to examine current and possible new mechanisms for preventing, deterring, and responding to development of biological weapons by states and other sophisticated actors, and to develop specific actions to address the root cause of states' decisions to pursue these weapons.

To this end, participants were asked to respond to specific questions throughout the exercise, including:

- What governance measures could meaningfully reduce biological risks associated with advances in technology?
- What global norms govern research and technology in the life sciences, including research involving pathogens with pandemic potential?
- What international capabilities and mechanisms are needed to deter or otherwise prevent the development of biological weapons by powerful actors, such as states?
- What international capabilities and mechanisms might be developed to attribute and effectively hold perpetrators accountable for the development, accidental release, or use of a biological weapon?

REPORT ORGANIZATION

The remainder of this report is organized into two parts: a summary of the discussions that took place during the exercise and a set of recommendations developed by the organizers to address the gaps and requirements identified through discussion among participants. NTI developed these recommendations after the event concluded; participants were not involved, and they have not endorsed them.

Overview of Exercise Discussion

Although the exercise was organized around a specific fictional scenario, the resulting discussion addressed a wide range of current, real-world challenges and their potential solutions. Most significantly, participants reached consensus regarding three major shortfalls in the global approach to biotechnology, biological weapons, and related risks:

1. The accelerating development, global spread, and accessibility of bioscience and biotechnology have not been matched with the development of norms and governance mechanisms to manage associated risks of deliberate misuse or accidental release.
2. The international community lacks robust transparency measures—and related systems of trust—to clarify the intentions and capabilities of bioscience research and development being conducted across the globe.
3. Internationally, there is a critical gap in capacity to rapidly investigate high-consequence biological events of unknown origin.

These shortfalls are discussed in greater depth below, followed by some additional considerations.

1. Rapidly Developing, Globally Distributed Life Science Research and Biotechnology

Tabletop exercise participants broadly agreed that there is a lack of international norms or governance mechanisms for life science research and biotechnology development, which would reduce emerging risks associated with this work. All participants agreed that continued biotechnology advances are vital for sustainable development, yet they also noted that the current environment poses significant risks of deliberate misuse and accidents.

Many life science researchers, for example, are unaware of the potential ways in which their research could be exploited for malign purposes, and the current international research-funding paradigm fails to promote risk reduction or prioritize the rigorous evaluation of potential biosecurity risks before funding and conducting research.

Participants agreed that while existing legal frameworks provide clear guidance for responding to deliberate misuse of bioscience, there is a normative and governance gap for well-intentioned research; this gap could either lead to an accidental release with potentially catastrophic global consequences or inadvertently enable malicious actors seeking to exploit this work for weapons development.

The underlying problem, as characterized by several participants, is that the international community lacks a shared view—or set of norms—about how to determine whether dual-use bioscience research and development activities should move forward, how to weigh the perceived benefits against potential safety or security risks, and how to mitigate risks if the work does proceed. For example, there is no international consensus about the boundaries that should

"...we do not have regulatory frameworks or any sort of governance at the global level. The only thing that's close is the World Health Organization Advisory Committee on Variola Virus Research, but we don't have anything like that at the global level for gain-of-function research."

— EXERCISE PARTICIPANT

be applied to certain dual-use life science research that enhances pathogen transmissibility, virulence, and/or resistance to medical countermeasures, but may offer benefits for development of medical countermeasures and other valuable tools.

Even if there were international norms, national governments, academia, and the private sector currently lack the means to codify or operationalize them. They lack clear and effective processes—or governance mechanisms—to oversee dual-use bioscience work from early-stage design and funding decisions, through project implementation, and on to publication. Although some national governments, academic institutions, and private organizations have set up governance mechanisms, variations in oversight for dual-use research currently create an uneven patchwork of biosecurity and biosafety practices and requirements across facilities, countries, and regions.

Several private-sector participants expressed surprise at the lack of international oversight and regulation of commercial technologies, such as DNA synthesis, as well as academic dual-use life science research,[2] including research that could enhance pathogen transmissibility, virulence, and/or resistance to medical countermeasures.[3] For example, in the area of DNA synthesis, it is increasingly difficult to evaluate the intended end use of commercially provided biological building blocks. As the discussion pivoted to identifying solutions for these challenges, participants suggested that policies that have been developed for the commercial sale of dual-use biomanufacturing equipment, such as fermenters and centrifuges, may serve as a model for future policies on commercial DNA synthesis or benchtop DNA synthesis devices.

The broader solutions to these challenges, several participants argued, is the development of norms at the international level. Others suggested that any solution must be underpinned by oversight and governance systems put in place by national governments, academia, and the private sector. The experts noted that this is a challenging task because the role of providing normative guidance and oversight for life science research and biotechnology development does not align well with the current mandate or capabilities of existing international organizations.

2 For example, only 5 percent of countries demonstrate that they practice oversight for dual-use research, including research with especially dangerous pathogens and toxins. Additionally, no government requires providers of synthetic DNA to screen their orders or prevent sharing of materials with questionable parties.

3 The following sources provide additional context and background on dual-use life science research:
https://easac.eu/fileadmin/PDF_s/reports_statements/Gain_of_Function/EASAC_GOF_Web_complete_centred.pdf
https://osp.od.nih.gov/biotechnology/gain-of-function-research/
https://www.phe.gov/s3/dualuse/Pages/GainOfFunction.aspx

Participants emphasized that the private sector must play a central role in addressing these challenges. Recognizing the growing leadership role of the private sector in advancing life science research and biotechnology development, participants cited the lack of specific guidance to govern their work. They agreed that although those who fund and conduct life science research outside of government typically do not focus on biosecurity, all of these organizations have a vested interest in safe and secure practices for such research around the world.

Given the private sector's leadership role in biotechnology development, participants suggested that this sector should also assume a greater leadership role in developing biosecurity measures and new governance approaches for their work, and recommended incentivizing them to do so.

2. Need for Transparency and Trust to Clarify Intentions and Capabilities

Rapid advances in biotechnology have also increased the need to enhance clarity and reduce the risk of misperceptions among states about the intent and capabilities of bioscience and biodefense research enterprises. Exercise participants emphasized that it is crucial to find new and concrete ways to build trust among nations and increase confidence that research intended to strengthen protections against deadly pathogens is not being misused or crossing the line into offensive work.

Without trust and stronger, more effective confidence-building measures, the international community continues to face the risk that misperceptions and suspicions could fuel state interest in the pursuit of bioweapons development in the future. In recent years, several governments have publicly expressed suspicion about the capabilities and intentions driving the bioscience and biodefense activities in other nations.

Current International Efforts

At present, the main international transparency mechanism for bioscience research and development is the Confidence-Building Measures (CBMs) system under the auspices of the Biological Weapons Convention (BWC). Many BWC States Parties have called for renewed efforts to develop a comprehensive and legally binding BWC verification regime, while other States Parties have argued that verification is not technically feasible and that such a regime would not provide an effective means of assuring compliance or improve national or global security. The concept of verification is currently locked in a political stalemate among BWC States Parties.

BWC CBMs consist of written reports about biological research and biodefense activities, which are submitted on an annual basis. Of the 183 BWC States Parties, 54 percent have not submitted a CBM in the past three years. BWC CBMs have remained largely unchanged for the past three decades. At the same time, a number of BWC States Parties have made suggestions to enhance CBMs. Previous attempts at establishing a more comprehensive transparency regime within the BWC have faced significant political and technical obstacles. The most recent serious attempt at developing a verification protocol began in the 1990s and ended in 2001.

"The nuclear industry understands that an accident anywhere impacts the entire industry. The same should go for the biotech industry. Is this a place for industry to lead, create transparency, and feed international mechanisms?"

— EXERCISE PARTICIPANT

Participants acknowledged the significant political and technical obstacles that have undermined previous international efforts in this area, but several stressed the importance of finding ways to make progress in this area.

Participants observed that governments, academia, and the private sector have an opportunity to take a fresh look at this set of issues and build a set of transparency-enhancing activities that the international community agrees are productive, which would enable these groups to transcend politically deadlocked conversations about verification.

While recognizing that there are clear, fundamental differences between biosecurity and other arms-control fields, several participants argued that lessons from nuclear security regimes might inform the development of new measures to increase transparency for bioscience research and development—especially dual-use research. Several participants pointed to the Additional Protocol for the Application of Safeguards,[4] which countries join on a voluntary basis and subsequently becomes legally binding. This agreement grants the International Atomic Energy Agency authority to conduct short-notice site inspections and to visit a broad range of facilities associated with the full life cycle of nuclear materials in peaceful use. The goal of these "complementary access" visits is to ensure that nuclear materials are not being diverted for weapons purposes, in keeping with national obligations under the Nuclear Non-Proliferation Treaty.

Through the BWC or even regional security arrangements, several participants argued, this model might provide a means to move beyond a purely voluntary set of transparency measures. While not all aspects of the Additional Protocol are salient in the context of transparency for bioscience research and development, some elements of this regime could serve as a model for developing more robust international tools that do not depend on full multilateral consensus as a starting point. For example, a group of states played an early leadership role by voluntarily adopting the Additional Protocol beginning in 1997 and subsequently advocating for more countries to join the regime. Over time, the Additional Protocol has evolved into a new de facto international norm in the nuclear arms-control arena, creating political pressure on the few countries that have remained outside the regime—including those suspected of noncompliance with their international obligations. In principle, it may be possible for a group of countries to launch an analogous initiative to bolster transparency and confidence in bioscience research and development.

4 See www.iaea.org/sites/default/files/infcirc540.pdf.

3. Managing the Interface between Public Health and Security During an Outbreak Investigation

Participants engaged in an in-depth conversation about ways to investigate suspected deliberate misuse or accidental release—as opposed to natural emergence—as the cause of a biological event of unknown origin. They discussed how a security investigation would interface with public health response efforts, as well as whether and how information would be shared between these two sectors. Exercise participants observed that a prompt determination of the origin of an outbreak during a public health crisis is extremely important for understanding the potential for re-emergence, gaining information about disease spread, and determining the availability of data that could assist with the development of medical countermeasures. However, they also acknowledged that tensions could arise between the need to collect public health data and save lives on the one hand and the need to collect information necessary for a security-focused investigation of a potentially unwilling suspect on the other.

The group discussed various approaches for compelling—or at least coaxing—a state that is suspected of such a violation to comply with ongoing investigations, cease any bioweapons-related activities, and share information that might be helpful for the public health response. Participants emphasized that the principal focus of any investigation would be to mitigate the loss of human life; however, they also noted that some sort of mechanism or body within the UN would be necessary to bring together disparate parties at senior levels to manage

the crisis by supporting an effective public health response, overseeing a prompt scientific investigation into the origin of the pathogen responsible for the event, and gathering information to objectively investigate suspicions of deliberate misuse or accidental release. Participants noted that technical missions would be critical for obtaining information about the source agent—including samples and testing records—especially

"In a crisis, you cannot wait. You have to send people in to secure the facility and see what is in the freezer. You many not learn more about the current outbreak, but you need to know if they just have poor laboratory practices or if they have malicious intent that is a threat to the world."

— EXERCISE PARTICIPANT

if preliminary work had been conducted to develop medical countermeasures. Access to facilities and records would also serve as a means of building confidence that the source of an accidentally or deliberately released biological event would not be used for "reload."

To meet these needs, participants discussed the importance of establishing an effective, internationally recognized mechanism for gathering security-relevant information in the early stages of a biological event that is suspected to have resulted from illicit biological weapons development and/or an accidental release. Participants noted that no existing international institution has the authority to play this role; it currently falls in the gap between the respective mandates of the WHO and the UN Office for Disarmament Affairs, and there is no centralized UN node to coordinate an effective international response and rapid investigation for high-consequence biological events of unknown origin.

Additional Considerations: The Importance of Robust Systems for Effectively Responding to Public Health Emergencies

By design, the exercise discussion was focused on emerging biological risks associated with rapid technology advances and on governance measures to meaningfully reduce these risks, as well as mechanisms for preventing, deterring, and responding to development of biological weapons by sophisticated actors, such as states. Yet the severe consequences in the fictional scenario drove many participants to also highlight the importance of strong health systems for an effective public health response. Participants repeatedly emphasized the role of systems and institutional mechanisms in mitigating and responding to biological events. Specifically, participants highlighted the need to invest in health systems early on to prevent the spread of disease during an outbreak.[5]

5 Although the critical importance of strong health security systems to mount an effective public health response was outside the scope of this exercise, NTI is focused on this issue and is working to bolster these systems through its work on the Global Health Security Index (www.ghsindex.org) and in calling for the establishment of a GHS Challenge Fund.

Recommendations

The NTI Tabletop Exercise on High-Consequence Biological Threats identified major gaps in norms and governance structures guiding biological research, international mechanisms to promote transparency and build trust around legitimate biological research, and international capabilities to investigate the source of a high-consequence biological event of unknown origin.

The bottom line: participants found that bioscience researchers lack norms to guide their work, especially when it ventures into risky territory. Moreover, there is no effective system to maintain trust and confidence among the international community that suspect governments—and parties in their countries—are not engaged in the development of offensive biological capabilities. Nor is there currently a viable, internationally respected mechanism to promptly investigate a suspicious outbreak of unknown origin during a global public health crisis.

NTI examined these three gaps and developed recommendations for each. The following recommendations reflect the views of the authors and should not be attributed to the participants in the exercise.

1. Reduce Biotechnology Risks and Implement Global Norms for Life Science Research

A UN agency or credible non-governmental institution should partner with experts from the scientific, philanthropic, security, and public health sectors to create an international entity dedicated to identifying and reducing emerging biological risks associated with technology advances and reducing global variations in oversight for dual-use life science research.

- The new entity would have two responsibilities: developing norms regarding the conduct of dual-use bioscience research and providing guidelines for the development of national, academic, and private-sector policies for governance of life science research and development, and associated commercial applications.
- The entity could be incubated and housed within an existing international organization or established as a new independent body with ties to existing international organizations.
- The WHO should consider expanding the purview of its Advisory Committee on Variola Virus Research to include research that enhances transmissibility and/or virulence of pathogens that have pandemic potential.

Life science funders should require and incentivize supported researchers to identify and reduce the risk of accidental or deliberate misuse in the design, conduct, and sharing of life science research and biotechnology.

- All life science research funders—including investors, philanthropies, companies, and governments—should embrace a Biotechnology Funders Compact that includes a commitment to conduct thorough biosecurity and biosafety reviews as part of their funding decision-making processes, as well as specific incentives to fund biosecurity and biosafety.
- Global commercial DNA synthesis and the sale of DNA synthesis machines should be governed by policies modeled after those in place for other dual-use technologies, such as fermenters and centrifuges.

2. Enhance Transparency to Build Trust and Reduce Uncertainty

International organizations, national governments, academia, and the private sector should develop and test a variety of enhanced transparency measures to reduce the risk of misperceptions about the capabilities and intentions of any nation's bioscience research and development activities.

- These measures should aim to reduce uncertainty about other states' capabilities and intentions regarding development of biological weapons and increase clarity about compliance with the BWC.
- In some cases, enhanced transparency measures might create opportunities for identifying potential problems with BWC compliance. However, an absence of evidence would not necessarily support high-confidence conclusions about compliance—that is, these measures cannot perform the full function of verification.
- Industry and academic research laboratories play a key role in innovative bioscience research and the engineering of biological systems and should take an active role in developing, testing, and implementing enhanced transparency measures.

New enhanced transparency measures could include written reports, scientific exchanges, site visits, research exchanges, and the creation of an informal venue for discussions about inconsistencies and ambiguities in the actions of others.

- As a concrete next step to advance this work, leaders in industry and academia

should develop a set of proposed enhanced transparency measures to pilot and iteratively refine. They could share their pilot project designs and experiences with each other to start to develop new best practices in this area.

- At the next BWC Review Conference in 2021, States Parties should advance this goal by including an agenda item about the development of Enhanced Transparency Measures in the work plan for the 2022–2026 Intersessional Process.
- The exercise organizers recognize that a number of national governments[6] have undertaken valuable work to advance these goals, including hosting voluntary peer review visits. Robust enhanced transparency measures should entail a much larger-scale effort that incorporates work led by a broader range of stakeholders, including industry, academia, and non-governmental organizations.
- Non-governmental organizations and other members of civil society focused on reducing biological threats posed by states and other sophisticated actors should conduct research and initiate consultations with a diverse group of international experts to explore the possibility of adapting salient aspects of the Additional Protocol to the IAEA Safeguards Agreements (or other potentially applicable arms-control measures) as a model for bolstering international transparency in the context of dual-use bioscience research and development.

3. Develop Capacity to Rapidly Investigate Biological Events of Unknown Origin

The international community should develop a new Joint Assessment Mechanism to enable a rapid-reaction multinational team to determine the source of a high-consequence biological event of unknown origin. This mechanism would address cases where there is ambiguity about the source of a biological event—specifically, whether it emerged naturally or was deliberately or accidentally released from an academic, commercial, or government laboratory.

- A Joint Assessment Mechanism would have an internationally diverse roster of technical experts and the operational capability to rapidly launch an investigation in response to a biological event of unknown origin—within 48 hours of authorization by the UN system.
- It would be more expansive and intensive than a standard WHO public health mission, and the bar for triggering it would be lower than that for a UN Secretary-General's Mechanism investigation.
- The process requirements for this trigger should be carefully calibrated. Triggering the Joint Assessment Mechanism should be rapidly achievable during a global public health emergency, and it should not be weighed down by onerous coordination requirements that lead to gridlock and inaction. That being said, the bar should be set high enough to preclude easy launch of frivolous

6 Countries that have played an important leadership role in developing and advancing voluntary peer review in the BWC context include Australia, Austria, Belgium, Canada, Chile, the Czech Republic, Georgia, Germany, Ghana, France, Luxembourg, Mexico, Morocco, the Netherlands, Spain, Switzerland, the United Kingdom, and the United States.

investigations that undermine the integrity of the mechanism.

- Architects of this mechanism should consider relevant financial, scientific, and human resources available within the UN system and among national governments.

The Office of the UN Secretary-General should designate a permanent facilitator or unit to develop the capacity for and lead a coordinated, multi-sectoral response to high-consequence biological events of unknown origin.

- A designated facilitator or unit should be given the resources and oversight to execute the Joint Assessment Mechanism described above.
- Because the facilitator or unit would need to be perceived as objective, a roster of experts to be part of a fly-away team should be designated in advance of an event.
- The mere existence of this facilitator or unit would serve as a deterrent.
- The position should reinforce the role of regional organizations, non-governmental entities, and multi-national corporations in seeking transparency by neighboring states.
- The position should oversee annual table-top exercises to stay abreast of emerging biological risks and iteratively test and strengthen UN and WHO capacity to marshal an effective, integrated response to high-consequence biological events from a range of sources.

Appendix A.
Expert Contributors to Scenario Development

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Appendix B.

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Appendix C.
Epidemiological Model Summary

Developed by Dr. Cassidy Nelson

The exercise scenario was modeled using Susceptible–Exposed–Asymptomatic–Infectious–Recovered (SEAIR) compartments based on ordinary differential equations. Four index cases in the fictional capital of Aplea started the outbreak. Following local domestic transmission, the disease spreads internationally via passenger airline flights, with infected cities around the world acting as seeders for their respective regions. All modeling was completed in the R software package.

The disease parameters for the scenario were derived using empirical data from H2N2 influenza viral outbreaks. The basic reproductive number (R_0) of 1.7 was chosen based on the 1957 H2N2 pandemic and used to calculate the transmission rate (β) for the scenario pathogen.[1] The incubation period was 1.9 days and the infectious period length was 2.49 days, based on published influenza studies.[2,3]

Within the norm for influenza outbreaks, two-thirds of cases showed symptoms.[4] The remaining cases were asymptomatic and had a 50% relative reduction in their infectivity.[5] The background immunity in the population to the virus was based on published data on global H2 viral immunity in different age groups (62% of people are immune if born before 1957, 21% immune if born between 1957 and 1968, and 0% are immune if born after 1968)[6] and combined with UN 2020 global demographic data.[7] This meant that globally, 10.6% of the population was fully immune to the virus at scenario beginning.

In the model, infection spread within and between cities and regions through the movement of infected individuals, with daily migration rates (η) based on UNWTO 2019 statistics.[8] By Day 45 in the scenario, countries had begun deploying non-pharmaceutical interventions. Hospital isolation of symptomatic individuals had the effect of moderately reducing their infectivity and chance of death through non-specific supportive medical treatment.

The overall fatality was 3% in the scenario, which is much higher than typical influenza outbreaks (<0.1%) but significantly lower than the estimated 10%–20% case fatality rate of the 1918 Spanish influenza pandemic (50-100 million deaths of approximately 500 million global cases).[9] Vaccination began on Day 240, with more than 8 million people immunized in the first month and 36 million individuals immunized within four months of the vaccine release.

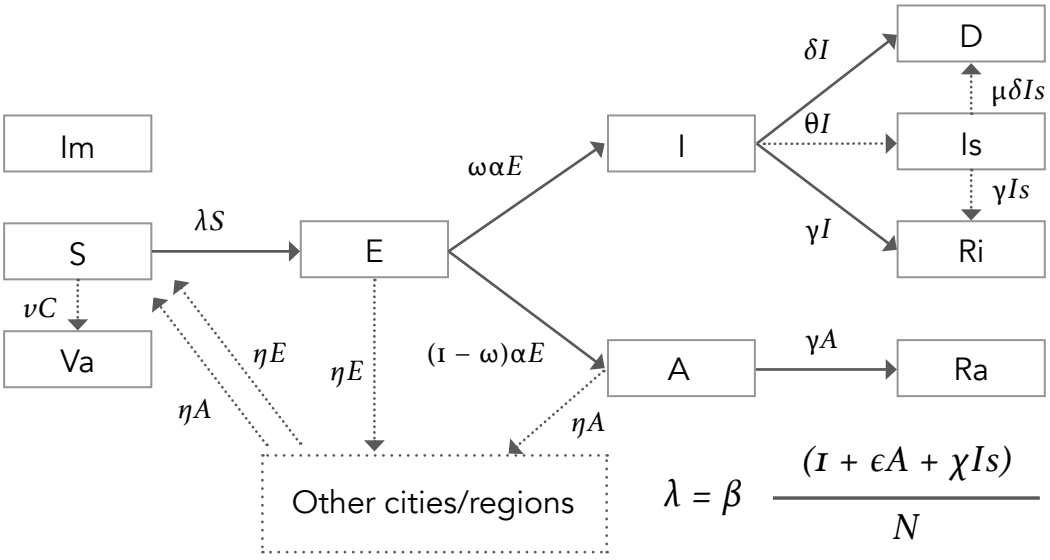
By the end of the scenario, more than 30% of the world had been diagnosed with the virus, comparable to the spread of the 1918 Spanish influenza pandemic, in which it was estimated that one-third of the global population had been infected.[9] More than 50 million people had died.

Table 1. Scenario model parameters and their values, with data sources specified

Parameter	Definition	Value	Source
β	Transmission rate	0·85	Calculated from H2N2 1957 Data[1]
ϵ	Relative infectivity of asymptomatic cases	0·50	[5]
χ	Relative infectivity of isolated symptomatic cases	0.75	Scenario
α	Rate of progression from exposed class (median incubation period 1.9 days)$^{-1}$	0.52	[2]
γ	Rate of progression to recovered class (mean infectious period 2.49 days)$^{-1}$	0.40	[3]
ζ	Case fatality rate	0.03	Scenario
ω	Proportion of exposed cases that become symptomatic	0.67	[4]
δ	Rate of progression to death among symptomatic infectious class	0·018	Calculated
θ	Isolation rate (after Day 45, prior to that it is 0)	0.02	Scenario
μ	Treatment effectiveness (1-relative reduction in mortality due to treatment)	0.90	Scenario
υ	Global vaccination rate per day (after Day 240, prior to that it is 0)	0.01%	Scenario
η	Migration rate between cities and regions (location dependent)	Various	UNWTO

Figure 1. Base compartmental model used for all cities and regions.

Compartments are represented as: Susceptible (S), Exposed (E), Asymptomatic (A), Infectious (I), Recovered (R_i and R_a), Isolated (I_s), Deceased (D), Vaccinated (V_a) and Immune (I_m). The force of infection (λ) is shown in the lower right corner, with N representing the population size. Remaining parameters are described in the table.



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About the Nuclear Threat Initiative

NTI is a nonprofit, nonpartisan global security organization focused on reducing nuclear and biological threats imperiling humanity. Founded in 2001 by former U.S. Senator Sam Nunn and philanthropist Ted Turner, who continue to serve as co-chairs, NTI is guided by a prestigious international board of directors. Ernest J. Moniz serves as co-chair and chief executive officer; Joan Rohlfing is president and chief operating officer.

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