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Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities

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Introduction

Over the past two years, breakthroughs in artificial intelligence (AI) have elicited constant commentary from technologists, policymakers, and pundits.[1] Far less attention has been devoted to a parallel revolution in biotechnology that permits the alteration of existing—and indeed creation of entirely novel—forms of life. That needs to change. The world is approaching a "ChatGPT moment" in biotech, thanks to dramatic innovations in gene editing and synthesis, themselves turbocharged by AI.[2] While these developments are well-known to specialists in the field, they are only dimly appreciated by many elected officials and policymakers, to say nothing of the general public.

Rapid advances in bioscience and bioengineering hold immense promise for human betterment. But as these disruptive technologies become more widely distributed—thanks in part to advances in machine learning that expand the frontiers of, and democratize access to, previously specialized knowledge—their inherently dual-use nature and susceptibility to unintended consequences could create unprecedented dangers.[3] Policymakers in the United States and abroad must address these risks today, so they are not caught flat-footed by the pace of technological advancement. This paper is intended as a primer of the main biosecurity and biosafety risks inherent in current trends—and priority steps to manage them.

The COVID-19 pandemic has been a painful reminder that we live in an epidemiologically interdependent world—and of the suffering, death, and disruption that virulent pathogens can wreak, regardless of whether they are naturally occurring, consciously engineered, or accidentally released.[4] In the wake of that experience, as well as other deadly zoonotic virus outbreaks including avian influenza (H5N1), Ebola, MERS, SARS, swine flu (H1N1), and Zika, governments and experts have proposed a slew of innovations to improve the world's

capacity to prevent, prepare for, detect, respond to, and recover from global public health emergencies.[5] These steps include establishing a global preparedness monitoring board, strengthening the legally binding International Health Regulations, creating new multilateral financial mechanisms (notably the Pandemic Fund), and continuing negotiations on a global pandemic treaty.[6] While progress remains uneven and tentative, United Nations (UN) member states have at least taken the threat seriously. What the multilateral system has *not* yet done is take commensurate steps to address the parallel dangers posed by dramatic advances in gene editing and synthetic biology.

To mitigate the risks of these emerging biotechnologies without squelching innovation, humanity will ultimately need new governance mechanisms at the global as well as national level to prevent the deliberate use of biological pathogens and minimize their unintentional release and unanticipated negative consequences. Unfortunately, the pace of discovery and development is fast outstripping the outdated, underpowered, and under-resourced multilateral arrangements that currently exist to promote biosecurity and biosafety. To begin closing these gaps, governments will need to bolster existing international frameworks, as well as create new ones, to detect, deter, prevent, and punish the malicious development and use of biological weapons by state and nonstate actors. They will also need to create more robust mechanisms to reduce the risks of catastrophic accidents. But all of these efforts must be pursued without strangling the dynamism of the biotechnology revolution and depriving humanity of its countless positive applications.

Two immediate priorities stand out. The first is strengthening the Biological Weapons Convention (BWC), the foundational multilateral treaty of the global biosecurity regime. Critical ingredients in that effort will include augmenting the meager resources and staff of the convention's implementing arm, institutionalizing new information-sharing and confidence-building mechanisms, strengthening the BWC's weak monitoring and verification provisions, expanding UN mechanisms to investigate potential violations, and holding countries accountable by imposing penalties on those that fail to fulfill their obligations, including through enhanced minilateral cooperation among like-minded governments. The second priority is managing the biosafety and biosecurity risks of the democratization of biotechnology. Critical objectives here include bolstering global standards for laboratories working with dangerous pathogens, introducing more stringent safeguards for DNA synthesis screening, and creating national and international guardrails to prevent AI systems from facilitating the production of bioweapons. None of these proposed reforms offers a proverbial silver bullet. But collectively, they would begin to correct the yawning imbalance between the risks posed by advanced gene-editing capabilities and the world's current meager defenses against catastrophic accidents and malicious actors seeking to exploit these cutting-edge technologies.

The Revolution in Genetic Engineering—and its Benefits and Risks

In 1987, Japanese scientist Yoshizumi Ishino encountered a peculiar pattern of repetitive DNA sequences in the *E. coli* genome, known in technical language as clustered regularly interspaced short palindromic repeats (CRISPRs), that help prokaryotes defend themselves from viruses.[7] Although he did not appreciate it at the time, Ishino's discovery would presage a biotechnology revolution. The application of CRISPR and its associated Cas9 enzyme, a technique pioneered by researchers Jennifer Doudna and Emmanuelle Charpentier, has provided scientists with history's most powerful gene-editing tool.[8] CRISPR-Cas9 has permitted the standardization and automation of genetic engineering, making it cheaper, faster, and more precise.[9]

Previously, the most common editing methods used nucleases to make site-specific cuts in DNA—a difficult and time-consuming procedure.[10] By contrast, the CRISPR-Cas9 system can be customized to target and edit stretches of genetic code at precise locations in any organism, and replace it throughout the genome in mere hours, not unlike the "command F" and "replace all" features of a Word document.[11] It has also expanded possibilities for synthetic biology: inserting new DNA sequences, whether found in nature or entirely novel, into an organism's genome. If done in the germ line (that is, reproductive cells)—rather than somatic cells (all others)—such changes can become heritable. Moreover, by employing the technology of gene drives, scientists can influence the reproductive fitness of particular genes (edited or naturally occurring), potentially altering the distribution of genotypes within given populations and indeed across entire species.[12]

Two decades ago, it took thirteen years and cost a staggering $2.7 billion to sequence the human genome.[13] Today, it can be done in under a day for just $600—a pace of progress that far exceeds Moore's Law (which posits that the speed and capacity of computers doubles every two years, thanks to advances in microchips and processors).[14] Biotechnology has also become a global undertaking, with labs and companies all around world, and yet we are nowhere near the apex of genetic engineering.

If anything, convergence of the biotechnology and AI revolutions promises a dramatic acceleration and democratization of gene-editing capabilities, allowing bioengineers to crunch enormous quantities of data, discern complex patterns outside the bounds of human cognition, and conduct automated experiments at a pace, scale, and efficiency that conventional trial and error laboratory science cannot hope to match.[15]

This convergence is well underway in the private sector. In August 2023, pioneering biotech firm Ginkgo Bioworks formed a partnership with Google Cloud to develop advanced large language models that would "supercharge our mission to make biology easier to engineer," in the words of Ginkgo's chief executive officer.[16] More recently, the biotech start-up EvolutionaryScale, founded by former Meta (Facebook) researchers, announced in

June 2024 that it had developed ESM3, the world's "first generative model for biology that simultaneously reasons over the sequence, structure, and functions of proteins."[17] Trained on over 2.7 billion proteins, ESM3 can generate new ones in response to prompts, analogous to word-generating chatbots such as Claude, Gemini, and ChatGPT. As Alexander Rives, EvolutionaryScale's chief scientist, explained, "We want to build tools that can make biology programmable."[18]

The potential benefits of these and other bioengineering breakthroughs are vast.[19] Synthetic biology and gene editing promise to transform medicine, materials science, manufacturing, consumer goods, agriculture, energy production, environmental protection, and so much more. They will revolutionize health, enabling more precise vaccines and therapeutics as well as personalized treatments for cancer, immune diseases, infertility, and metabolic disorders. They will advance sustainable development, including by making crops more resilient and food production more efficient, as well as accelerate the clean energy transition, including by introducing new biofuels and harnessing the power of natural organisms such as algae to mitigate climate change. Already, the practical applications of bioengineering innovation range from curing sickle cell disease to modifying the cow gut microbiome to release less methane, a powerful greenhouse gas.[20]

The revolution underway in the life sciences is a Promethean moment. Armed with growing understanding of the encoding and regulatory functions of genes, scientists now have the capacity to manipulate and shape their expression in biological organisms from single-celled eukaryotes to humans themselves.[21] Alongside incredible rewards, however, this awesome power poses serious and growing risks that need to be managed. Two of the most important are the dangers of malevolent use and unintended consequences.

Bioweapons and Bioterrorism

Gene editing and gene synthesis technologies are inherently dual use, meaning they can be employed for good or ill by sovereign states, nonstate groups, and even individuals. This dual-use dilemma is nothing new.[22] From prehistory to the present, humans have invented tools, from hand axes to drones, that can cause grave damage in the wrong hands. What sets gene editing and synthetic biology apart are their theoretical potential to cause suffering and death on a massive scale, including by making viruses more transmissible and lethal and by creating entirely new organisms that can be tailored to target specific groups of people (as well as, conceivably, agricultural commodities, natural ecosystems, and critical species). Such dangers are likely to grow as gene-editing capabilities become more distributed and as advances in AI and machine learning allow would-be attackers to create more deadly pathogens and determine more effective and efficient means to deploy them.

Although the likelihood of an engineered pathogen wiping out humanity remains vanishingly low, the risk of mass-casualty attacks will inevitably grow as the technical knowledge to create such weapons spreads.[23] One could imagine a scenario whereby a national government

or a terrorist group causes catastrophic damage by intentionally releasing a plague among an adversary's population—or even humanity at large—that has limited or no immunity. One tabletop exercise conducted by Johns Hopkins University suggested that an engineered bioweapon could kill up to 150 million people worldwide.[24] For these reasons, bioweapons are often classified as one of several catastrophic and existential risks facing humanity, alongside nuclear war, runaway climate change, adversarial artificial general intelligence, the explosion of a supervolcano, or the planet's collision with a near-Earth object (such as an asteroid).[25]

Biological weapons have been used periodically throughout history—from the Bronze Age days of the Hittites, an Anatolian people who reportedly sent rams infected with tularemia into enemy villages, to the Seven Years' War, when British troops allegedly exposed France's Native American allies to smallpox by gifting them blankets infected with the virus.[26] The weapons' most notorious deployment occurred in the mid-twentieth century, during the Sino-Japanese War and World War II. Soon after occupying Manchuria in 1931–1932, the forces of Imperial Japan developed a biological warfare program.[27] Code-named Unit 731, it ultimately tested cholera, anthrax, and other diseases on Chinese and Korean prisoners of war.

During the Cold War, the United States and the Soviet Union each developed and maintained significant biological warfare programs, and Moscow concealed at least two accidental outbreaks. The first occurred in 1971 when smallpox escaped from a Soviet bioweapons facility near the Kazakh town of Aralsk, killing three and infecting many more.[28] In 1979, an anthrax outbreak at another illicit Soviet bioweapons production facility killed seventy residents of the surrounding city of Sverdlovsk.[29] The U.S. government assesses that Russia and North Korea maintain clandestine offensive bioweapons programs today, in violation of their treaty obligations under the BWC.[30]

Despite this record, many strategists have long regarded anxieties about the state-sanctioned use of biological weapons to be overblown, given their marginal military utility.[31] Such instruments are inherently imprecise, the thinking goes, since pathogens can infect friend and foe alike, making it difficult to contain their ghastly effects. U.S. president Richard Nixon voiced this sentiment in 1969, in publicly renouncing their development and use by the United States: "Biological weapons have massive, unpredictable, and potentially uncontrollable consequences," he declared.[32]

While Nixon's calculus may have been true at the time, the convergence of biotechnology and AI innovation may require a new risk assessment.[33] Because AI can be trained to generate detailed designs of historical and novel pathogens as well as to identify, link, and correlate genetic information and markers across and within populations, governments (and potentially terrorists) may soon find it easier to design more virulent and precise bioweapons targeted at specific ethnic groups or even individuals.[34] This may provide some context to the February 7, 2022, meeting between Russian President Vladimir Putin and his French counterpart Emmanuel Macron, who had traveled to Moscow in a last-ditch effort to persuade the Russian leader not to invade Ukraine. Upon arrival, Macron declined to submit to a COVID-19 test, for fear that his genetic information might be stolen and misused.

The two leaders proceeded into a five-hour meeting, sitting at opposite ends of a six-meter conference table.[35] Within the U.S. national security community, there is growing concern that adversarial nations, particularly China, will employ AI to generate targeted virulent and transmissible pathogens, including ones not found in nature.[36] In a context of geopolitical mistrust and lack of transparency, it is easy to imagine an escalatory spiral between these two superpowers, fueled by misinformation and disinformation.

The democratization of biotechnology also increases the risk of bioterrorism. Globally, individuals and private groups increasingly have access to sophisticated tools and materials for genome editing. While this diffusion of expertise and capability will accelerate innovation, it is also likely to lower barriers to entry for mass-casualty terrorism by making it easier for nonstate actors to obtain or engineer dangerous biological agents in a manner difficult to detect or prevent.[37] The result, some counterterrorism experts fear, could be "a new age of bioterror," in which malicious actors use gene-editing tools to fine-tune the transmissibility, targeting, and lethality of viral agents.[38]

The world is no stranger to bioterrorism, though it has to date thankfully been modest in scale. In 1984, the Oregon-based Rashneesh cult sickened 751 people in Oregon by contaminating ten salad bars with the salmonella bacteria.[39] A decade later, the Japanese doomsday cult Aum Shinrikyo attempted an anthrax attack in Tokyo. (When that failed, the group turned to sarin gas, launching an assault on the city's subway system that killed twelve passengers and injured at least 5,000.)[40] In September 2001, microbiologist Bruce E. Ivins killed five Americans and harmed seventeen more by mailing letters containing deadly anthrax spores.[41] To be sure, Ivins was a U.S. government employee with access to a biosafety level (BSL)-4 lab containing some of the world's deadliest pathogens.[42] It is conceivable, however, that a future extremist individual or group could also obtain dangerous biological materials, whether by isolating these from infected animals or contaminated soil, stealing them from a research laboratory or bank, purchasing them from a sympathetic scientist or rogue government official, or even reverse-engineering them through gene synthesis.

Until recently, many experts had discounted the last of these possibilities as implausible, since it would require a nonstate actor to obtain the entire genome sequence of a virus and design a targeted biological weapon.[43] However, the diffusion of scientific knowledge and the rise of AI may warrant a reassessment.[44] In testimony to the U.S. Senate last year, Dario Amodei, the cofounder and chief executive officer of Anthropic, stated that AI advances may provide unskilled individuals with the ability to create large-scale biological attacks within two to three years.[45]

Three decades ago, Aum Shinrikyo could only inflict as much harm as nature permitted. Soon, a similar group could use AI and new gene synthesis techniques to engineer deadly pathogens far beyond evolutionary constraints, targeted at specific individuals or groups.[46] And unlike states, which can generally be compelled to behave rationally out of fear of exposure and retaliation, motivated bioterrorists will be harder to deter, particularly if they have a millenarian mindset. Al-Qaeda, it should be noted, researched and conducted

rudimentary experiments with biological pathogens and presumably would have had few scruples in using them as weapons.[47] More recently, in 2018, German authorities in the city of Cologne foiled a plot by a jihadi terrorist group that had succeeded in producing ricin.[48] According to Lawrence Kerr, former director of pandemics and emerging threats at the U.S. Department of Health and Human Services, the U.S. intelligence community at one point had identified "3,000 named apocalyptic groups around the world," any number of which might be comfortable with the annihilation of some or all human beings.[49]

Biosafety Risks: Accidents and Unintended Consequences

Beyond actions with intent to harm, mistakes and mishaps could bring misfortune. Genetic engineers often lack complete understanding of the function and effects of specific genes, meaning that modified organisms intentionally released into nature could have deleterious effects on humans, other species, and ecosystems. Moreover, if scientific knowledge is imperfect, scientists are even more so. Among the greatest biosafety fears is that a dangerous pathogen might accidentally escape containment, harming people, other organisms, or the environment.

Of particular concern are accidents involving gain-of-function (GOF) research, which involves changing genetic material to induce new or enhanced capabilities in microbial organisms, typically viruses.[50] Under controlled conditions, GOF experiments can help researchers better understand human-pathogen interactions and drug resistance, as well as prepare for future pandemics and develop countermeasures. In one 2024 study, for example, researchers at Northwestern University engineered a deadly pathogen to destroy itself from the inside out, using synthetic biology to bypass its natural defense mechanisms.[51] Still, the expression and impact of viral mutations and modifications can be unpredictable, varying drastically depending on its particular (lab or natural) setting.[52] A single genetic alteration in a virus can affect more than one trait, for example by enhancing its replication capabilities while impairing its ability to evade the immune system (or vice-versa).[53]

Human error could also have dire consequences in GOF research.[54] Lab accidents occur frequently: someone breaks a glass, rubs their eye, slips and falls, or sets the wrong temperature. In September 2016, a Washington University graduate student was alone in her BSL-3 laboratory, working to develop a vaccine to chikungunya, a mosquito-borne virus, when she accidentally pricked her finger with the needle.[55] She awoke a few days later with a fever, debilitating body aches, and discolored spots on her skin. Only upon diagnosis did she report the accident to the National Institutes of Health (NIH), which registered it with the hundreds of other incidents that occur annually in U.S. labs.[56] The stakes in this incident, involving only one person and a vector-borne illness, were minor compared to a lab accident involving a highly virulent and easily transmissible pathogen released during GOF research. The ongoing, heated debate over COVID-19's origins reflects credible concerns that the virus could have escaped from a BSL-4 lab only blocks from the wet market in Wuhan, China, where it was first documented.[57] Regardless of the virus's proximate origins, the episode underscores the risks posed by GOF research designed to enhance pathogen functions.

Closing Gaps in Global Biosecurity and Biosafety Regimes

There is no integrated, comprehensive global framework to govern the risks posed by bioengineering. Rather, there is a nascent "regime complex," comprising a messy array of overlapping multilateral treaties, organizations, institutions, and networks, as well as multistakeholder and industry groupings.[58] The components of this complex include among others:

- the BWC, which prohibits the development, production, stockpiling, acquisition, and retention of microbial and other biological agents and toxins that have no peaceful purposes, as well as of related equipment and means of delivery;[59]
- the Australia Group, a voluntary partnership among forty-two countries (and the European Union) designed to harmonize export controls on dual-use materials and technologies to prevent the proliferation of bioweapons;[60]
- UN Security Council Resolution 1540 (2004), which prohibits and seeks to prevent the transfer to nonstate actors of weapons of mass destruction and related technologies;[61]
- the Global Health Security Initiative (2001), an informal partnership among the G7 countries and Mexico to strengthen global preparedness and response capacity for pandemic influenza and WMD, including biological weapons;[62]
- the Cartagena Protocol on Biosafety (2003), an addendum to the Convention on Biological Diversity (CBD) governing the transnational movement of living modified organisms;[63]
- the Nagoya Protocol (2014) to the CBD, which promotes access to and benefit-sharing of the utilization of genetic resources;[64]
- the World Health Organization (WHO), which has issued recommendations and a framework for governance of human genome editing;[65] and
- the International Biosecurity and Biosafety Initiative for Science, a new independent organization dedicated to reducing risks associated with life sciences research, particularly misuse of DNA synthesis technology.[66]

The speed of biotechnology innovation is outpacing these governance efforts, however. Spectacular advances in gene editing and synthetic biology, accompanied by dramatic breakthroughs in artificial intelligence and machine learning, risk opening the door for state governments and malicious nonstate actors to create or modify deadly, naturally occurring viruses or even synthesize entirely new ones and deploy these as biological weapons.

Given space constraints, the remainder of this paper does not attempt a comprehensive assessment of this entire regime complex. Rather, it focuses more narrowly on two major priorities for advancing biosecurity and biosafety: strengthening the BWC and creating guardrails to combat risks inherent in the democratization of gene-editing technology. The latter efforts should include creating more robust international arrangements to safeguard high-risk laboratories, more tightly regulating DNA synthesis screening, and preventing malevolent actors from using AI to create bioweapons.

Strengthening the Biological Weapons Convention

One of humanity's signal achievements in the otherwise violent twentieth century was the negotiation of an absolute prohibition on biological weapons. The BWC, which entered into force on March 26, 1975, was the culmination of decades of diplomacy.[67] Half a century earlier, with the horrors of the Great War still fresh, member states of the League of Nations had approved the Geneva Protocol (1925), a short document ostensibly outlawing "the use in war of asphyxiating, poisonous or other gases, and of bacteriological methods of warfare."[68] Alas, as the historical recap above suggests, the protocol's impact on actual state conduct was negligible. And it took a half-century for the world to replace the protocol with something more robust.

The BWC—formally known as The Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction—was the first multilateral treaty to outlaw an entire class of weapons. It has proven remarkably resilient. While many other international treaties, from the Genocide Convention (1951) to the Chemical Weapons Convention (1997), have been repeatedly violated over the decades, the taboo against the use of biological weapons has stuck as one of the most important and observed norms in world politics.[69] This is partly a reflection of the unique revulsion and opprobrium such weapons elicit. They are, in the words of the BWC itself, "repugnant to the conscience of mankind."[70] It is also a function of their perceived lack of military utility to date.

Unfortunately, the BWC, which turns fifty next spring, is showing its age.[71] Rapid technological advances and rising geopolitical tensions are eroding the foundations of this global prohibition regime by lowering the barriers to developing or acquiring such weapons and potentially altering the calculations of state and nonstate actors alike. Declining levels of trust among great powers, as well as a degraded global information environment, also increase the risk of misperceptions—as well as temptations to lodge false accusations. (In March 2022, for instance, the Kremlin sought to defend the Russian invasion of Ukraine by accusing the United States of conducting dangerous experiments in a secret network of biolabs in that country).[72]

In the face of these trends, the BWC is underpowered and underresourced. Let's begin with its budget and staff, which are risibly small. In 2023, the BWC's total budget amounted to just $2.1 million—less than the average cost of a two-bedroom apartment in Manhattan.[73] The BWC has 183 states parties, but two-thirds of these governments pay annual dues of less than $1,000 apiece—roughly half of what the average American spends annually on gasoline. Meanwhile, the BWC's chief oversight mechanism, the Implementation Support Unit (ISU), has only *four* permanent staff (albeit up from just three in 2022).[74] Given its tiny funds and few personnel, the ISU relies heavily on voluntary contributions of technical assistance from wealthier countries to help poorer ones meet their treaty commitments.

These paltry figures stand in stark contrast to the ample budgets and personnel available to the main international organizations created to control nuclear and chemical weapons. The International Atomic Energy Agency (IAEA), which supports peaceful uses of nuclear energy and maintains international safeguards against nuclear proliferation, boasts an operating budget of $387 million and 2,497 professional and support staff.[75] Likewise, the Organisation for the Prohibition of Chemical Weapons (OPCW), created in 1997 to oversee implementation of the Chemical Weapons Convention (CWC)—which like the BWC prohibits parties from developing, producing, acquiring, stockpiling, retaining, transferring, or using this entire category of weapons—has an $83.5 million budget and a workforce of 500.[76] For the BWC to fulfill its mandate, the ISU's tiny budget and staff must grow.

The BWC's most crippling weakness is its lack of any legally binding verification mechanism to ensure compliance with its provisions. The ISU has no power to monitor treaty implementation by states parties. Here again, the contrast with chemical and nuclear weapons regimes is striking. The CWC contains rigorous provisions for intrusive on-site verification, permitting the OPCW to monitor chemical industries to prevent development of prohibited weapons. (In July 2023, the OPCW confirmed that the United States, the last declared possessor of such weapons, had irreversibly destroyed its stockpiles).[77] Moreover, under Articles IX and X of the CWC, states parties can in principle request challenge inspections of any state to investigate alleged weapons use.[78] Members of the OPCW inspection team have the authority to inspect any areas and to collect samples for analysis, without hindrance—a significant qualification of sovereign prerogatives.[79]

The verification provisions of the nuclear nonproliferation regime are also extensive. Since the entry into force in 1970 of the Treaty on the Non-Proliferation of Nuclear Weapons (NPT), all nonnuclear weapons states have been obliged to negotiate comprehensive safeguards agreements with the IAEA, which has authority to monitor and inspect their nuclear facilities to verify that nuclear material is not diverted to weapons programs but used only for peaceful purposes.[80] Following revelations of illicit nuclear programs in North Korea and Iraq in the early 1990s, the IAEA in 1997 adopted a Model Additional Protocol, which expanded the agency's authority and capacity to investigate clandestine nuclear facilities. As of 2021, 153 countries had signed the protocol, more than 700 nuclear facilities worldwide were under safeguards, and the IAEA had conducted more than 2,000 inspections.[81]

In an ideal world, states parties would negotiate a similarly robust, legally binding BWC verification mechanism. In the real world, however, such a framework may prove elusive, given the democratization of access to bioscience innovations and the dual-use dilemmas associated with biotechnology, which are even more daunting than for nuclear and chemical weapons.[82] To begin with, the materials and techniques needed to create bioweapons are frequently the same as those used in peaceful bioscience applications, making it difficult to ascertain whether the relevant organisms and technologies are being used for good (for example, developing a new vaccine) or ill (for example, creating a more lethal pathogen). Generally speaking, it is easier to distinguish between peaceful and nonpeaceful uses of nuclear and chemical materials and related equipment.

Second, biological weapons are inherently harder to trace. The effects of man-made pathogens can resemble natural disease outbreaks, making their origins difficult to pinpoint.[83] Such programs are also easier to conceal, because bioweapons—which consist of self-replicating organisms and can be effective in very small quantities—require far less space to produce and stockpile.[84] By contrast, nuclear weapons programs require extensive infrastructure and fissile materials that can be difficult for even a sovereign government to obtain, while chemical weapons programs involve the production of huge volumes of chemical agents, many of which have no legitimate purposes and thus can be banned with fewer complications.

Given these difficulties, many experts wonder whether a robust regime for monitoring and verification is even plausible.[85] Imagine, for example, that a newly created ISU verification team randomly selects the BSL-4 lab in Belarus for an on-site visit.[86] Upon inspection, they find that a team of scientists is engineering a deadly strain of tick-borne nairovirus. When the ISU interrogates the research team, the lead scientist calmly explains that they are simply studying the virus's evolution in order to create a vaccine for the lethal Crimean-Congo hemorrhagic fever.[87] The challenge for oversight then becomes distinguishing between bioweapons development and peaceful research grounded in legitimate public health objectives.

Lacking any real mechanisms to monitor, verify, and enforce compliance with its principles and prohibitions, the BWC today is essentially a gentleman's agreement, rather than a real bulwark against purposeful harm. As such, it risks being overwhelmed by new capabilities borne of the information technology revolution and the global proliferation of bioscience interests and applications.

Pathways to BWC Reform

Parties to the BWC have been seeking to strengthen the convention for three decades, with only limited success. In 1994, an ad hoc group of UN member states began talks on a legally binding additional protocol that would require enhanced transparency of national biological facilities and activities to reduce the risk of violations. Its proposed core provisions would include "mandatory declarations of dual-use activities and facilities; routine visits to

declared facilities, without specific evidence of a treaty violation; and short-notice challenge investigations, requested by a member state, of a suspect facility, an alleged use of biological weapons, or a suspicious outbreak of disease, so as to address concerns about possible non-compliance."[88]

As these negotiations proceeded, however, diplomats dropped the word "verification" entirely, replacing it with dozens of calls for "transparency."[89] Several months after taking office in January 2001, the administration of U.S. president George W. Bush rejected the draft protocol entirely and withdrew from negotiations, contending that the envisioned instrument would be ineffective in deterring determined proliferators while hampering legitimate research, facilitating commercial espionage, and undermining U.S. national sovereignty.[90]

More recently, prior to the last BWC review conference (RevCon) in 2022, the administration of U.S. President Joe Biden indicated willingness to reopen the question of verification, restoring some momentum to previously scuttled negotiations. "For the past two decades," U.S. delegation head Bonnie Jenkins declared, "efforts to strengthen the Convention have been treading water," even as the biological weapons threat had grown.[91] To help usher the BWC into the twenty-first century, she called on states parties to "establish a new expert working group to examine possible measures to strengthen implementation of the Convention, increase transparency, and enhance assurance of compliance."

Ultimately, the 2022 RevCon proved disappointing. Although the U.S.-proposed working group was established, the gathering failed to generate even rudimentary agreement on verification measures, thanks to Russian and Iranian resistance and the rule that all decisions be taken by consensus. The meeting also failed to create an international science and technology body to serve as a repository of the latest developments in the biological and life sciences, or to endorse the Chinese-supported Tianjin Biosecurity Guidelines for Codes of Conduct for Scientists.[92]

In lieu of a verification mechanism, BWC parties have had to make do with a set of confidence-building measures designed to reduce misperceptions and suspicions. These measures encourage states to self-report their relevant activities in response to detailed questionnaires. However, the measures remain voluntary, have a low participation rate, and fail to capture many relevant national capabilities and private sector innovations in biotechnology and bioscience.

To help correct these flaws, the Nuclear Threat Initiative (NTI)—a nonprofit global security organization working to reduce nuclear, biological, and technology threats—has proposed several constructive reforms to enhance transparency of the global biosecurity regime.[93] These include encouraging more detailed national assessments of evolving bioscience and biotechnology capabilities, involving a broader range of nongovernmental stakeholders in national assessment and self-reporting processes, providing the ISU with greater resources to analyze national submissions, and introducing a rigorous system of voluntary peer review. (The last of these would be analogous to peer review mechanisms created in other spheres,

such as the Enhanced Transparency Framework for the Paris Climate Agreement and the Universal Periodic Review mechanism for the UN Human Rights Council).[94]

Beyond increased trust and transparency, a genuine BWC verification regime will ultimately require more robust mechanisms to monitor compliance, investigate possible violations, and hold lawbreakers accountable for their actions.[95] At present, the BWC has no instruments of its own for these purposes, meaning that any country that suspects a violation would need to rely on complementary arrangements.[96] One potential framework is the UN Secretary-General's Mechanism for Investigation of Alleged Use of Chemical and Biological Weapons, comprising a roster of experts and labs, funded by a smattering of wealthy governments.[97] The secretary-general has activated this mechanism on three occasions with respect to alleged chemical weapons use, but never (so far) for biological weapons. Another possible instrument is the WHO, which would presumably help lead a response to any high-consequence biological event. But its comparative advantage lies in investigating naturally occurring outbreaks, rather than bioweapons use. To help fill this gap, NTI has proposed that the office of the UN secretary-general create a new Joint Assessment Mechanism for biological incidents.[98]

Another more ambitious option would be to create a fully-fledged international body to support the BWC, capable of rapidly deploying experts to investigate the suspected use of biological weapons. In a September 2020 address to the opening of the UN General Assembly, the president of Kazakhstan, Kassym-Jomart Tokayev, called for the establishment of an International Agency for Biological Safety (IABS), analogous to the IAEA, to support the BWC.[99] As formally presented to BWC states parties in August 2021, the new body would seek to create a universal multilateral export control regime consistent with Australia Group principles; "create a system of checks and guarantees" to ensure that biotechnology is "used for peaceful purposes only"; set up a UN register of scientific discoveries that might be used for military purposes; "compile and analyze annual mandatory reports/declarations" on confidence-building measures; provide technical assistance to help states detect and combat biological threats; promote common standards and regulations for biosecurity and biosafety; exchange information on biological incidents; and coordinate requests for emergency assistance.[100]

However, in the current geopolitical environment, creating a fully-fledged intergovernmental organization like the proposed IABS would be a heavy diplomatic lift, as it would require consensus among the world's major powers, including the United States and its Western allies, on the one hand, and China and Russia, on the other. In the interim, one promising strategy for countries genuinely committed to strengthening biosecurity commitments and accountability would be to adopt a dual-track approach to international cooperation that balances participation within the universal BWC framework with more ambitious "minilateral" efforts among a like-minded coalition of nations. The United States and other Western countries are no strangers to this strategy, having frequently formed selective, high-ambition coalitions to avoid the pitfalls of encompassing UN settings that are often held hostage by recalcitrant nations and produce lowest-common-denominator outcomes.[101] A prominent

example is the global Financial Action Task Force, established by the United States and Western allies to combat money laundering (and subsequently terrorist financing).[102]

Another such entity is the International Partnership Against Impunity for the Use of Chemical Weapons, established in January 2018 by forty states and the European Union in reaction to chemical weapons use by the government of Syria and the self-proclaimed Islamic State.[103] Among other commitments, its adherents agree to compile and share all relevant information regarding use of chemical weapons and to designate, sanction, and where possible bring to justice governments, groups, and individuals responsible for perpetrating such crimes. One could imagine a similar minilateral entity, anchored among but not limited to Western nations, that complements and bolsters the BWC by ensuring that there are actually consequences rather than impunity for any development and use of biological weapons.[104]

Managing the Safety and Security Risks of the Biotech Revolution

Beyond complicating multilateral nonproliferation and arms control efforts, the democratization of access to cutting-edge genetic engineering technologies and the emergence of a flourishing global bioeconomy increases the risks of both catastrophic accidents and bioterrorism.[105] Mitigating these growing safety and security risks will ultimately require new governance arrangements at both the national and international level, including novel oversight mechanisms, regulatory institutions, and standards of conduct for private as well as public sector actors.[106]

At the international level, three regulatory priorities stand out: strengthening global biosafety and biosecurity standards for laboratories researching and manipulating the most dangerous pathogens to reduce the likelihood of accidents or diversion; tightening and universalizing requirements for DNA synthesis screening to make it harder for malicious actors to obtain or fabricate genetic sequences of concern; and establishing AI guardrails to prevent terrorists from exploiting machine learning to design, develop, and deploy biological weapons.

Back in 1975, when the BWC was just entering into force, a group of 140 scientists, physicians, lawyers, journalists, and government officials gathered at the Asilomar Conference Center in Pacific Grove, California, to discuss risks posed by recent breakthroughs in recombinant DNA research, which allowed for the mixing of genetic material from distinct organisms.[107] The meeting, organized by pioneering biochemist Paul Berg and several other leading researchers, produced a set of voluntary research principles and guidelines intended to mitigate possible biohazards.[108] These included containment standards for laboratory trials and prohibitions on certain high-risk experiments, such as "the cloning of recombinant DNAs from highly pathogenic organisms" as well as of "DNA containing toxin genes."[109]

In the ensuing decades, national governments adopted diverse approaches to the oversight and regulation of biotechnology, including with respect to genetically modified organisms.[110] Given the relatively immature state of the field, these distinct regulatory approaches to risk were manageable (though they did create diplomatic headaches, even among erstwhile allies).[111] Today, as the pace of biotechnology innovation accelerates and barriers to entry continue to fall, the limitations of these ad hoc, uncoordinated approaches are becoming more apparent.

At the time of Asilomar, scientists still faced significant scientific, technological, and financial hurdles to manipulating genetic material. Those impediments, as noted, have shrunk. The dissemination of gene-editing techniques, the growing availability of genetic sequences and other experimental materials, and the increased availability of sophisticated computing, engineering, and robotics capabilities have vastly increased the number of people who have access to once-specialized knowledge, restricted material, and know-how—potentially allowing groups or even individuals to create new pathogens or resurrect old ones of high lethality, such as the variola (smallpox) virus or the 1918 influenza virus. In other words, the genie is out of the bottle.[112]

The democratization of biotechnology is evident in the rise of a do-it-yourself (DIY) community of genetic engineering enthusiasts and biohackers who employ gene-editing techniques to reengineer DNA outside of traditional laboratory settings.[113] While the vast majority of such activities are benign, the rise of "nonconventional genetic experimentation" has understandably raised biosecurity and biosafety concerns.[114] How long, one wonders, before the teenager next door is in his basement experimenting with the next lethal pathogen like smallpox, using a DIY CRISPR gene-editing kit he got online for just $179?[115]

Thankfully, creating and deploying deadly viruses remains beyond the reach of the vast majority of amateur genetic engineers. Accomplishing such a feat would require access to specific genetic material, specialized scientific knowledge and technical skills to manipulate and create the desired pathogen, and possession of high-end equipment and financial and other resources to be able to weaponize and deliver it.[116] Still, these hurdles seem destined to fall, thanks in part to AI. Already, some amateur enthusiasts have succeeded in synthesizing dangerous viruses.[117] Discouraging such risky activities will require new legal frameworks and stronger self-policing within the growing community of genetic engineers. One promising model for the latter is iGEM, an independent, nonprofit organization that encourages young scientists to experiment with synthetic biology in responsible ways.[118]

Meanwhile, the global bioeconomy has exploded, presenting enormous opportunities but also potential risks. In 2023, the value of the worldwide biotechnology market exceeded $1.45 trillion; by 2032, its valuation could more than triple to $4.5 trillion.[119] Governments have taken notice. In the United States, both the administrations of Biden and former president Donald Trump hosted major summits on the bioeconomy, touting the transformative potential of biotech and biomanufacturing innovations across an array of economic sectors and activities, including promising applications in health, agriculture, bioremediation,

manufacturing, materials science, energy production, and more.[120] In September 2022, Biden signed an Executive Order on Advancing Biotechnology and Biomanufacturing Innovation, envisioning massive investments in "foundational scientific capabilities" and other steps to ensure that the United States dominates and shapes the rules of the emerging bioeconomy.[121] An important (if unspoken) motivation for U.S. policy is to outcompete the People's Republic of China, which is also investing heavily in this sector. Beyond economic competitiveness concerns, many U.S. national security officials worry that Beijing views biology as a new domain of warfare.[122] This suspicion—whether warranted or not—is exacerbated by China's lack of transparency.

A dilemma for the United States and other like-minded countries is to create governance frameworks that strike the right risk-management balance, allowing biotechnology research and private sector innovation to thrive and deliver positive applications while minimizing the safety and security vulnerabilities inherent in the dispersal of such powerful new tools. This quandary is front and center in Biden's 2022 Executive Order, which envisions harnessing AI and other computing tools to seize new biotechnology opportunities and bring innovative products to market. "We need to develop genetic engineering technologies and techniques to be able to write circuitry for cells and predictably program biology in the same way we write software and program computers," the president writes.[123] At the same time, he acknowledges, "We must take concrete steps to reduce biological risks associated with advances in biotechnology," by investing in biosafety and biosecurity as well as promoting "ethical and responsible uses" that are congruent with "the public good" and "consistent with respect for human rights."

Sharpening this dilemma is an inherent tension between the responsibilities of national authorities and the economic incentives of private corporations. National authorities, of course, have a fundamental obligation to advance the public interest by safeguarding the safety, security, and well-being of citizens. Corporations, by contrast, are self-interested entities motivated by profit; as such, they have a very different risk calculus than governments and prefer self-policing over regulatory burdens. Similar dynamics, of course, are visible in ongoing domestic U.S. debates over the nature of AI risks—and how to manage these.[124]

Over the past quarter century, the United States has taken important domestic steps to address emerging biosecurity and biosafety risks at home.[125] In the wake of the high-profile anthrax attacks of September 2001, Congress passed the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, directing the Secretary of Health and Human Services (HHS) to establish, maintain, and periodically update a list of so-called "select agents," or biological agents and toxins with a "potential to pose a severe threat to public health and safety."[126] The resulting U.S. Federal Select Agent Program placed stringent safeguards and security measures on the possession, use, or transfer of these materials, and the U.S. Centers for Disease Control and Prevention created a federal registry requiring all workers at facilities in possession of select agents to state their holdings and undergo background checks.[127] In 2005, the Bush administration created a National Science Advisory Board for Biosecurity, a twenty-five member panel of experts reporting to the Secretary of

HHS designed to assess the dual-use risks of federally funded biotechnology research.[128] A decade later, following the publication of controversial experiments to increase the transmissibility of avian influenza, HHS increased its oversight of GOF experiments involving genetic manipulation and modification to alter the virulence, transmissibility, or functioning of pathogens.[129] The U.S. government has also published a set of guiding principles to ensure "institutional compliance with biosafety, biocontainment, and laboratory biosecurity regulations and guidelines."[130]

While such security and safety concerns persist, there is also a growing and noteworthy conviction among U.S. politicians and policymakers—presumably driven by a combination of competitiveness concerns, geopolitical calculations, and private sector lobbying—that such risks must be managed in a way that promotes rather than squelches U.S.-led scientific innovation. This ethos permeates the 2022 National Biodefense Strategy, but it is especially noteworthy in the work of the National Security Commission on Emerging Biotechnology, established by Congress as part of the National Defense Authorization Act of 2022.[131] The commission's broad remit includes analyzing trends in biotech innovation and investment, assessing a range of associated security risks, and proposing strategies to ensure that the United States dominates cutting-edge biotechnology.

The commission is slated to submit its final report to Congress in December 2024. Its interim report, published in January 2024, offers a rosy assessment of the field, arguing that "new biotechnologies . . . paint an exciting picture for the future."[132] At the same time, the commission recognizes that maintaining U.S. biotechnology leadership and achieving U.S. national security goals cannot be achieved by unilateral means alone and that existing international oversight mechanisms are incommensurate with growing biosecurity and biosafety risks from gene editing and synthetic biology. Accordingly, the commissioners endorse "international engagement and collaboration with friends, allies and likeminded countries;" multilateral efforts to harmonize diverse national approaches to safety and security; the promotion of "international norms and standards for biotechnology that align with U.S. values and ethics;" and the bolstering of global supply chains for biotechnology and biomanufacturing.

When it comes to malevolent use, the commission strikes an optimistic note, suggesting that "emerging technologies may themselves provide the technical capabilities to preempt, detect, and mitigate misuse concerns."[133] For example, new approaches to "wastewater surveillance could help with early detection of biological threats."[134] This presumption—that biotechnology itself will allow authorities to anticipate and counter the biosecurity and biosafety risks created by its misuse—is widespread among biotechnologists, and understandably so. After all, any effective response to the deployment of an engineered pathogen will inevitably require at least three types of medical countermeasures in which biotechnology is front and center, namely "detection via diagnostics, treatment via therapeutics, and prevention through vaccines."[135]

However, a prudent approach to managing the risks of the bioengineering revolution must rest on more than techno-optimism. It should also entail reducing some obvious vulnerabilities created by the diffusion of gene editing and synthetic biology to private, nonstate actors. This approach will necessarily be very different from conventional nonproliferation efforts based on "guns, gates, and guards," notes Gigi Kwik Gronvall of Johns Hopkins University.[136] "It is not possible to wall off biotechnologies to prevent their misuse or to hold information related to biotechnology secret."[137] Mitigating dual-use risks will require sovereign nations to adopt multilayered, multistakeholder governance frameworks that integrate the public sector, private industry, and academic research units—and to launch multilateral efforts to harmonize the disparate domestic approaches they adopt to govern their biotech sectors and laboratories.

Achieving such global cooperation will be difficult. As participants in a 2020 NTI global bio-incident simulation concluded, "the international community lacks a shared view—or a set of norms—about how to determine whether dual-use bioscience research and development activities should move forward, how to weigh perceived benefits against potential safety or security risks, and how to mitigate risks if the work proceeds."[138] To cite just one example, nations currently exhibit varying levels of tolerance for GOF research—a field of inquiry that may help the development of medical countermeasures against known pathogens but could also create dangers, particularly if pathogens under experiment escape containment. Complicating matters, existing national-level regulatory frameworks to govern dual-use research across companies, government labs, and academic institutions tend to be fragmentary, reducing the coherence of domestic (to say nothing of international) governance.

Notwithstanding these obstacles to international coordination, national governments can and should take three near-term steps to improve global cooperation to reduce the potentially catastrophic risks of the biotechnology revolution.

Strengthen and harmonize biosafety and biosecurity standards for labs. Globally, the number of laboratories where scientists study deadly human and animal diseases is growing quickly.[139] According to the war studies department of Kings College London, as of 2023, there were fifty-one BSL-4 labs worldwide—double the number a decade ago—spread across twenty-seven countries.[140] Another three were under construction and fifteen more were planned, mostly in Asian nations such as India and the Philippines. In such facilities, scientists work with lethal contagious pathogens and toxic agents with a high risk of aerosol transmission and against which there are no effective vaccines or therapies. More than 60 percent of these facilities are government-run public health institutions, and three-quarters are in urban settings, raising concerns about epidemic risk should any pathogen escape containment. In addition, the world has another fifty-seven operating "BSL-3+" labs, particularly in Europe, where scientists also study highly pathogenic viruses such as avian influenza.

Unfortunately, current measures to address the biosafety and biosecurity risks of such research appear to be uneven. According to the Kings College study, twenty-one out of

twenty-seven countries with BSL-4 labs score high on biosafety governance (with four nations—India, Côte D'Ivoire, Gabon, and Saudi Arabia—scoring very low).[141] By contrast, only twelve out of twenty-seven countries with BSL-4 labs score high on biosecurity. Most alarmingly, only *one* country out of twenty-seven, Canada, scores high on dual-use research governance, as measured by the existence of statutory legislation regarding oversight of research involving dangerous pathogens of pandemic potential. As the authors conclude, "the post-COVID building boom in BSL-4 labs is so far not matched by accompanying biorisk management policies." More generally, observes Lawrence Kerr, while there is growing appreciation that the world needs stronger standards for BSL-3 and BSL-4 labs, "We don't actually have any entity that is now responsible for those types of norms globally," nor any agreement as to where the locus of those standards should be.[142] Kerr asks the question on everyone's mind: "Does it reside at the United Nations? Is it something that's within the remit of the World Health Organization?"

An ideal long-term solution for plugging this gap would be for parties to the BWC to negotiate the creation of a fully-fledged international agency to support the convention, analogous to the IAEA or the OPCW, with the authority to inspect existing BSL-4 and BSL-3+ facilities to ensure that they implement adequate biosafety and biosecurity safeguards. Given the aforementioned diplomatic obstacles to creating such an agency, however, the international community will likely need to look elsewhere in the near and medium term when it comes to reducing lab-related biorisks. One option would be to leverage the convening and standard-setting functions of WHO, which in 2022 released a Global Guidance Framework for the Responsible Use of the Life Sciences: Mitigating Biorisks and Governing Dual-Use Research, and which maintains a network of regional offices.[143] The WHO's combination of normative leadership and on-the-ground presence leaves it well-positioned to foster the emergence of a global biorisk management network, including encouraging peer reviews of national laboratories.[144] The organization is no stranger to this general role, having long hosted the Advisory Committee for Variola Virus Research, created by the World Health Assembly in 1999 to oversee research using the live virus that causes smallpox and to conduct biosafety and biosecurity inspections of the two repository sites in Russia and the United States.[145]

In combination with these universal multilateral efforts, the United States and other like-minded governments can pursue narrower minilateral approaches to encourage high laboratory standards.[146] As noted earlier, such arrangements can allow participants to move faster and avoid spoiler dynamics and lowest-common-denominator outcomes, while advancing higher standards to which other countries can gradually subscribe. The Financial Action Task Force, for instance, began as a G7 initiative but has since seen its distinctions between "cooperating and non-cooperating" jurisdictions become a de facto global standard.[147] One could imagine a similar coalitional framework to promote high standards for biolabs, classifying jurisdictions according to how their facilities rank on particular criteria, such as the biorisk management standards for labs set in 2019 by the International Organization for Standardization (ISO 35001).[148]

Bolster and universalize standards for DNA synthesis screening. A second priority for managing risk in the burgeoning bioeconomy is to create robust frameworks for DNA synthesis screening to make it more difficult for would-be bioterrorists to create dangerous pathogens in labs.[149] In recent years, benchtop DNA synthesis devices have become important tools for legitimate biotechnology research, including in the fields of cancer, cell biology, and infectious disease. In the wrong hands, however, these devices could also be used to engineer lethal pathogens with pandemic potential. Although the United States maintains stringent regulations and export controls on labs that work with sixty-eight dangerous microbes and toxins designated as "select agents," DNA synthesis devices can in principle allow scientists to assemble and reproduce such pathogens in laboratory settings.

With an eye to reducing this risk, NTI and the World Economic Forum (WEF) in January 2020 proposed "a new common global mechanism" that would help corporations that provide customers with nucleic acids "screen DNA orders—to ensure that the building blocks of dangerous pathogens don't fall into the hands of malicious actors."[150] Most companies that supply such materials already screen synthetic gene orders, as participants of the (now thirty-odd member) International Gene Synthesis Consortium, founded in 2009.[151] The NTI-WEF initiative would strengthen and universalize this practice.

The proposal has garnered significant support, not least in the United States. In October 2023, HHS issued new guidance to companies that provide synthetic nucleic acids.[152] Beyond reaffirming that suppliers should check customer requests against the U.S. list of "select agents," it calls for enhanced screening "to encompass all sequences that are recognized to contribute to pathogenicity or toxicity as information regarding these sequences and their verified functions and improved screening methods become available." The guidance also advises manufacturers of benchtop devices capable of synthesizing "sequences of concern" (SOCs) to distribute these only to "customers whose legitimacy has been verified" and to "implement mechanisms to track legitimate use of their equipment." Building on this guidance, the White House on April 29, 2024, released a new Framework for Nucleic Acid Synthesis Screening. It mandates that "recipients of federal R&D funds . . . procure synthetic nucleic acids only from providers that implement these best practices."[153] The framework further directs the National Institute of Standards and Technology to work with industry and other stakeholders "to refine best practices "for effective nucleic acid synthesis procurement screening," particularly of SOCs. Providers and manufacturers are also instructed to adopt know-your-customer practices and to report potentially illegitimate purchase orders of SOCs or of benchtop synthesis equipment.

These are welcome developments, creating strong financial incentives for companies who do business with the U.S. federal government to comply with federal guidelines.[154] Still, important gaps remain. Most obviously, the new guidelines create new obligations only for DNA providers and synthesis machine manufacturers engaged with the U.S. government. It will take an act of Congress to codify into law best practices for all DNA synthesis screening, as well as common standards for hardware and software safeguards for DNA synthesizers.

Second, as the National Security Commission on Emerging Biotechnology notes, "There is no universal consensus on the set of sequences that merit concern, beyond those known to code for certain pathogens."[155] The advent of AI complicates this dilemma by raising the possibility that nefarious actors could use machine learning tools to design entirely novel DNA sequences that screeners have (by definition) never seen but are nevertheless dangerous.

Third, at the global level, there is no comprehensive multilateral effort afoot to create a worldwide regime for DNA synthesis screening. This provides an opening for bad actors to engage in regulatory arbitrage by evading high-standard jurisdictions such as the United States and seeking out countries where screening requirements are weak or nonexistent.

In an effort to begin closing this gap, at the February 2024 Munich Security Conference, NTI launched the International Biosecurity and Biosafety Initiative for Science (IBBIS), an independent organization headquartered in Geneva dedicated to reducing risks from bioscience research, with an initial focus on "prevent[ing] the misuse of DNA synthesis technology."[156] As a centerpiece of that effort, IBBIS is developing "an international Common Mechanism for DNA synthesis screening," an open-source software tool that helps providers of DNA and RNA ensure that the material and technology they provide is not exploited for malevolent purposes.[157] While IBBIS is a welcome institutional development, global biosecurity and biosafety will ultimately depend on a robust multilateral governance framework for DNA synthesis screening that complements the initiative's work.

Establish AI guardrails to reduce the risks of bioterrorism. The revolution in gene editing is not occurring in a vacuum, but rather alongside accelerating advances in artificial intelligence. Among national security professionals and some technologists, there is growing anxiety that AI may dramatically lower the threshold for malicious actors to construct destructive biological weapons.[158] Armed with machine learning technologies, complex algorithms, and massive computing power, terrorists could in principle increase the virulence of existing pathogens and develop blueprints for entirely novel ones that are more infectious, transmissible, and even targeted at the genetic makeup of specific individuals or human groups, as well as of plants, animals, and other organisms. To be effective, any oversight framework for bioengineering will thus need to address the convergence of these two suites of technologies.

The relevant time horizon for this growing artificial intelligence and biotechnology (AIxBio) threat remains a matter of debate. In January 2024, the RAND Corporation published the results of a red team study, in which investigators posing as "malign nonstate actors" attempted to use advanced AI models to plan a biological attack. The team concluded that "biological weapon attack planning currently lies beyond the capability frontier of LLMs [large language models]."[159] The same month, an internal study by OpenAI reached a similarly reassuring conclusion: "In an evaluation involving both biology experts and students, we found that GPT-4 provides at most a mild uplift in biological threat creation accuracy," compared to what is readily available on the internet.[160]

Skeptics have challenged these optimistic (and, in the case of OpenAI, arguably self-serving) assessments.[161] But regardless of *current* capabilities, the seemingly inexorable advance and dispersion of AI and bioengineering technologies suggests that malicious actors may well obtain the capabilities to design, develop, and deploy sophisticated and destructive bioweapons in the near future.[162]

When discussing the risks of AIxBio convergence, it is worth distinguishing between two types of AI tools, which could in principle be used separately or in combination.[163] The first type comprises LLMs such as ChatGPT, which could help individuals or groups obtain specialized scientific information and data, make biologically relevant predictions, or conduct simulations that aid in the creation of a virulent biological agent.[164] Under this scenario, chatbots could help nefarious actors design the next pandemic pathogen or targeted bioweapon.[165]

The second less familiar AIxBio pathway would be for a malevolent actor with significant scientific training to employ not a natural language chatbot but rather an AI-enabled biological design tool such as GSM3 "to more effectively generate new pathogen designs, develop synthetic DNA strands that subvert screening guardrails, or improve the efficiency of bioweapon production."[166] As generative biology applications become commonplace, the world will indeed have entered a ChatGPT moment for bioengineering. Already, well-intentioned scientists have used AI "to simulate chemicals with increased toxicity and to design algorithms for pharmaceuticals that could also be used as biochemical weapons to disrupt diverse bodily functions."[167]

A logical first step to reduce these biosecurity and biosafety risks would be to encourage leading AI technology firms to embrace industry-wide guardrails that prevent or at least complicate this scenario. In summer 2023, the White House secured voluntary commitments from fifteen leading AI companies to test and red-team their systems prior to release to guard against major sources of misuse and risk, including related to biosecurity.[168] Not long after, G7 governments meeting in Hiroshima, Japan, in October 2023, adopted an International Code of Conduct for Organizations Developing Advanced AI Systems. This voluntary guidance calls on all relevant corporations and organizations to identify, evaluate, and mitigate a wide range of dangers, chief among them "chemical, biological, radiological, and nuclear risks, such as the ways in which advanced AI systems can lower barriers to entry, including for nonstate actors, for weapons development, design, acquisition, or use."[169]

Holden Karnofsky of the Carnegie Endowment for International Peace has proposed that AI model developers adopt voluntary, "if-then" limitations in testing their most powerful AI models before release to prevent those models from crossing unacceptable redlines.[170] No AI, he rightly notes, should permit users to obtain step-by step instructions for creating a weapon of mass destruction, whether a functioning nuclear device or a virulent pathogen. In principle, if-then commitments would require developers to ensure that if an AI develops dangerous capabilities, specific trip wires and risk mitigation procedures are in place to reduce or eliminate the associated dangers. As of summer 2024, sixteen leading

AI companies had announced their intent to establish specific redlines and related if-then commitments ahead of the Paris AI Summit in February 2025.

In principle, an industry-wide commitment to redlines and if-then commitments could begin to reduce the risk posed by AIxBio convergence, at least with respect to LLMs. The caveat to this is that voluntary redlines are not necessarily transparent, accountable, or enforceable. This is disturbing, giving indications that the leaders of some technology companies—including OpenAI—appear to be running roughshod over their safety teams, suggesting that voluntary commitments will easily be trampled if profit is at stake.[171]

Beyond the issue of model safety, technology companies need to devote more attention both upstream and downstream to ensure that AIxBio convergence does not unwittingly create biosecurity and biosafety risks. Upstream, they need to protect and secure biological data that could be used to build a biological design tool. Downstream, companies must commit to stringent postrelease monitoring and enforcement of their own platforms to identify and stop dangerous uses—a practice that remains uneven today.[172]

Self-regulation, however, should only be the beginning. Public authorities in the United States will need to ramp up their tentative regulatory efforts to mitigate the risks of genetic engineering and synthetic biology. The White House Executive Order on AI, released on October 30, 2023, mandates that companies report to the government when developing models above a certain threshold.[173] (Significantly, that threshold is three orders of magnitude *lower* for models trained on biological data). Meanwhile, U.S. state governments, led by California, are debating imposing their own regulations. In late August 2024, the California State Assembly and Senate overwhelmingly passed a sweeping AI safety bill, (SB-1047), over the ferocious resistance of many Silicon Valley firms. If signed into law, it would have made technology companies legally liable for "critical harms," explicitly including mass-casualty biological events.[174] Governor Gavin Newsom ultimately vetoed the legislation, arguing that it would have placed onerous burdens on the state's leading AI companies.[175] The episode is surely only the opening salvo in a looming regulatory battle.

More fundamentally, national governments will need to develop—and ideally harmonize at the multilateral level—strategies to mitigate the dangers of the AIxBio era. The United States has already taken tentative steps in this direction. In April 2024, the U.S. Department of Homeland Security (DHS) released a major report on reducing risks at the intersection of AI and weapons of mass destruction.[176] Among other recommendations, the report endorses (1) more detailed federal guidance to private actors on the public release of source codes and model weights for biologically focused AI models and design tools, (2) limits on access to sensitive biological data from publicly accessible databases, (3) know-your-customer provisions for companies providing nucleic acid synthesis, and (4) the identification of "chokepoints" to mitigate or contain biological risks along the "digital-to-physical frontier." The report also advocates greater engagement with foreign governments, international organizations, industry, civil society organizations, and other stakeholders to develop common "approaches, principles, and frameworks to manage AI risks."

Finally, the DHS report emphasizes the need to develop tailored AI tools to mitigate the very risks that AIxBio convergence has unleashed, including when it comes to identifying, deterring, and interdicting malevolent actors; detecting anomalous disease outbreaks; designing, developing, and deploying vaccines and other medical countermeasures against novel pathogens; and monitoring state and nonstate compliance with international agreements.[177] Such a "defensive" use of AI to counter biological risks is already underway, albeit in a piecemeal fashion, as evident in the new partnership between Moderna and OpenAI to advance mRNA medicine.[178]

Conclusion

Next year will mark a half a century since the BWC's entry into force and the convening of the Asilomar conference—two historic milestones in humanity's ongoing efforts to address the dual-use risks posed by biotechnology. Fifty years on, dramatic advances in gene editing and synthetic biology, turbocharged by parallel advances in AI, have transformed the biosecurity and biosafety landscape. On the positive side, breakthroughs in bioscience, engineering, and machine learning are making it possible to program the building blocks of life, resulting in an ever-growing list of innovative applications that promise to better the human condition. More negatively, the democratization of bioengineering capabilities has lowered the barriers to entry for malevolent state and nonstate actors seeking to develop and deploy targeted bioweapons and has increased the risk of unintentional, catastrophic accidents.

The daunting task for policymakers in the United States and abroad is to establish new governance frameworks that will allow humanity to reap the benefits of this scientific innovation and the growing bioeconomy, while also protecting itself from bioweapons, bioterrorism, and bio-accidents. Unfortunately, the pace of scientific advancement is outstripping existing governance arrangements, creating significant biosecurity and biosafety vulnerabilities that threaten to overwhelm the benefits of the bioengineering revolution.

Mitigating the dual-use risks of gene editing and synthetic biology will require important institutional reforms at both the national and international level. One obvious priority is bolstering and supplementing the underpowered BWC, which despite its shortcomings remains the institutional centerpiece and normative heart of the multilateral regime complex for countering biological weapons. Besides dramatically expanding the budget and staff of its ISU, states parties must continue efforts to negotiate new monitoring and verification provisions under the BWC.

It goes without saying that the current geopolitical climate is hardly conducive to such a diplomatic breakthrough, much less the creation of a fully-fledged intergovernmental organization analogous to the IAEA or OPCW. Accordingly, governments should also pursue more modest, parallel efforts to enhance the transparency of the global biosecurity

regime, including through (among other steps) the introduction of a rigorous system of peer review and greater reliance on the office of the UN secretary-general to investigate and assess alleged possession or use of biological weapons. Finally, the United States and like-minded governments should adopt a two-track approach to biological security, complementing their participation in the encompassing BWC framework with the pursuit of more ambitious goals within a narrower minilateral coalition of governments anchored among but not limited to Western nations. The history of global governance testifies to the potential of high-ambition coalitions to establish principles and norms that subsequently become embedded as international standards.

Simultaneously, national authorities must take steps both individually and collectively to address the growing bioterror and biosafety risks inherent in the democratization of cutting-edge gene-editing technology, without undermining the dynamism of the surging bioeconomy and the many positive commercial applications that it promises to deliver. Three priorities are front and center. First, to reduce the prospect of accidents and diversion, governments must tighten safety and security safeguards at research laboratories where scientists are conducting work on the planet's most dangerous pathogens. Second, to ensure that sequences of concern are not unintentionally provided to bioterrorists, they must work with the private sector to create more robust DNA synthesis screening procedures. The ultimate goal should be to create a comprehensive, multilateral regime to prevent the misuse of DNA synthesis technology, building on the IBBIS model. Finally, authorities must work with private corporations to create guardrails that prevent malicious actors from exploiting AI, including biological design tools, to create and use biological weapons. Beyond encouraging corporate self-policing and deploying economic incentives to influence behavior, national governments will likely need to impose mandates to ensure that private companies act in the public interest.

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