DEFENSE, EMERGING TECHNOLOGY, AND STRATEGY PROGRAM

Securing the Biotechnology Frontier

Three Targeted Technical Interventions to Strengthen US Biodefense in the Post-Pandemic Era

Anemone Franz

HARVARD Kennedy School
BELFER CENTER

50 YEARS OF RESEARCH, POLICY, AND LEADERSHIP

JULY 2025

Belfer Center for Science and International Affairs
Harvard Kennedy School
79 JFK Street
Cambridge, MA 02138

www.belfercenter.org

DEFENSE, EMERGING TECHNOLOGY, AND STRATEGY PROGRAM

Securing the Biotechnology Frontier

Three Targeted Technical Interventions to Strengthen US Biodefense in the Post-Pandemic Era

Anemone Franz

HARVARD Kennedy School
BELFER CENTER
50 YEARS OF RESEARCH, POLICY, AND LEADERSHIP

JULY 2025

About the Defense, Emerging Technology, and Strategy Program

The Defense, Emerging Technology, and Strategy Program examines defense policy and the role of emerging technologies in shaping international security. For more, visit belfercenter.org/programs/defense-emerging-technology-and-strategy.

About the Author

Anemone Franz is a German physician and recent graduate from the Harvard T.H. Chan School of Public Health. She completed her medical education at the University of Würzburg in Germany, where she conducted her doctoral research on parasitic infections in sub-Saharan Africa at the Würzburg Institute for Global Health. Following graduation, she worked as a clinical trial physician at Alvea, a start-up company developing vaccine platforms, and served as an advisor for the non-profit organization 80,000 Hours. During her time at Harvard, she worked on dual-use research governance at the Harvard Center for Communicable Disease Dynamics. Anemone was selected as a 2024 Emerging Leaders in Biosecurity Fellow at the Johns Hopkins Center for Health Security and is a member of the European Leadership Network. As an incoming 2025 Horizon Fellow, she will continue her work on biosecurity, dual-use research governance, and emerging technology governance in Washington, DC.

Acknowledgements

I would like to thank Byron Cohen, Aaron Maiwald, Joshua Monrad, Jess Rogers, Nikki Romanik, and Eric Rosenbach for comments on the manuscript and helpful discussions, and Britney Tran for her help editing the draft. All remaining mistakes are my own.

Table of Contents

Associated Press, Frank Augstein

Executive Summary

While the COVID-19 pandemic initially brought the extreme human and economic costs of natural infectious diseases to the public's attention, the ongoing lab leak debate has shifted the focus to an equally concerning threat: the possibility of engineered pandemics. Rapid advancements in biotechnologies have democratized capabilities once limited to high-resourced laboratories, creating an urgent need for governance frameworks that balance competitive innovation with strong national and global biosecurity. As technological advances continue to outpace regulatory oversight, the post-pandemic world faces a critical inflection point where our choices about biosecurity governance will shape our defences against future threats and our ability to harness biotechnology's life-saving potential.

The COVID-19 pandemic has fundamentally altered attitudes toward biological research governance. While determining the origins of SARS-CoV-2 remains important, the central debate often misses a more crucial point: the mere possibility of a laboratory release, regardless of whether it occurred in this instance, reveals critical vulnerabilities in our biosecurity and biosafety systems.

This policy brief proposes **three targeted technical interventions** to strengthen America's resilience to biological threats and safely develop and deploy cutting-edge biotechnologies:

1. **Enhance DNA Synthesis Screening and Verification:** Strengthen and build upon existing frameworks to establish comprehensive federal screening requirements for all DNA synthesis orders to prevent misuse of this critical technology.
2. **Advance Pathogen Early Warning Systems:** Deploy cutting-edge surveillance technologies and unified data platforms that can detect emerging biological threats earlier and more reliably than current systems.
3. **Improve Genetic Engineering Detection and Attribution Capabilities:** Develop technical forensic capabilities to determine if pathogens have been engineered and potentially trace them to specific laboratories.

These technical interventions would collectively strengthen America's biodefense capabilities to prevent, detect, and attribute biological threats, creating a defense against natural outbreaks and engineered pathogens. By investing in these critical technologies, the United States can establish global technical standards, create new high-value industries, and ensure that biotechnology's transformative potential benefits humanity rather than threatening it.

Understanding Today's Biosecurity Challenges

The Promise and Potential of Biotechnology

Biotechnology represents one of the most promising technological frontiers. Applications for novel biotechnologies span healthcare, agriculture, materials science, and environmental protection. According to a recent National Security Commission on Emerging Biotechnology (NSCEB) report, "by 2030, most people on the planet will have consumed, used, worn, or been treated by a product of emerging biotechnology." This isn't just a scientific revolution but an economic one: biomanufacturing is projected to be used extensively in more than a third of traditional manufacturing industries by the end of this decade, representing nearly $30 trillion in global value.[1]

The health applications alone are transformative. CRISPR gene therapies now offer cures for previously untreatable conditions like sickle cell disease, while gene drive technologies show promise for controlling malaria by modifying mosquito vectors.[2] CAR T-cell therapy has achieved remarkable cancer treatment success, with 62% five-year remission rates in previously virtually untreatable leukemia patients.[3] Estimates suggest that 45% of the global disease burden could be

1 "NSCEB-Full-Report---Digital--4.28.Pdf," accessed May 9, 2025, https://www.biotech.senate.gov/wp-content/uploads/2025/04/NSCEB-Full-Report-%E2%80%93-Digital-%E2%80%934.28.pdf; "Synthetic Biology Is About to Disrupt Your Industry," BCG Global, February 8, 2022, https://www.bcg.com/publications/2022/synthetic-biology-is-about-to-disrupt-your-industry.

2 Kubendran Naidoo and Shüné V. Oliver, "Gene Drives: An Alternative Approach to Malaria Control?," Gene Therapy 32, no. 1 (January 2025): 25–37, https://doi.org/10.1038/s41434-024-00468-8; Office of the Commissioner, "FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease," FDA (FDA, September 8, 2024), https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.\\uc0\\u8221{} {\\i{}Gene Therapy} 32, no. 1 (January 2025

3 "CAR T Cell Therapy: A Remarkable Breakthrough in Cancer Treatment," accessed May 9, 2025, https://www.wolterskluwer.com/en/expert-insights/car-t-cell-therapy-a-remarkable-breakthrough-in-cancer-treatment.

addressed with existing biotechnologies, arguably making investment in this sector not just an economic imperative but an ethical one.[4]

Furthermore, the exceptional promise of medical breakthroughs positions biotechnology as a strategic priority in great-power competition. Beyond treating disease, these technologies can enhance national security through bioresilience, rapid diagnostics, and countermeasures against both natural and engineered biological threats. Maintaining leadership in this field is therefore essential, not only for public health and economic growth, but also for national security.

The Dual Use Dilemma

While synthetic biology represents one of humanity's most promising scientific frontiers, the same tools that enable scientists to develop life-saving therapies for previously incurable diseases can also be used by bad actors to cause harm. Research aimed at understanding dangerous pathogens to develop countermeasures could inadvertently generate information that bad actors could misuse to make those pathogens more lethal or transmissible. Similarly, the same platforms designed to create novel therapeutics could be repurposed to engineer biological weapons. This so-called "dual-use dilemma", where the same research can lead to both beneficial applications and harmful misuse, creates complex governance challenges.[5]

This tension is exacerbated by the diverse and often competing interests of key stakeholders. Academic researchers tend to value open science, transparency, and the free exchange of information to accelerate discoveries. Commercial entities seek intellectual property protection to secure returns on research investments. Security experts advocate for oversight mechanisms and potential restrictions on particularly concerning research activities or information sharing. Public health officials focus on maximizing benefits while minimizing risks across populations. Each stakeholder brings a legitimate perspective to the table, which should be considered when finding balanced governance approaches.

4 "NSCEB-Full-Report---Digital--4.28.Pdf."

5 "Postpn340.Pdf," accessed May 9, 2025, https://www.parliament.uk/globalassets/documents/post/postpn340.pdf.

Technical Advances Lowering Barriers to Access

The convergence of artificial intelligence and biotechnology increases biotechnological capabilities and may lower technical barriers—creating both unprecedented opportunities and serious security concerns. Tools like AlphaFold from Google's DeepMind have revolutionized protein structure prediction, compressing what once took months or years into a weekend's work.[6] When combined with gene-editing technologies like CRISPR, these advances enable scientists to design novel biological systems with unprecedented precision and speed.

The pace of progress in this domain outstrips even Moore's Law. In 2003, the Human Genome Project first sequenced the entire human genome in thirteen years, at a total cost of $2.7 billion.[7] Today, it can be done in under a day for just $600.[8]

Evo 2, the largest AI model for biology to date, developed by the Arc Institute in collaboration with NVIDIA, is a salient example of how machine learning can accelerate biological research. This open-source AI tool, trained on the DNA of over 100,000 species, "can predict the form and function of proteins in the DNA of all domains of life and run experiments in a fraction of the time it would take a traditional lab".[9] Evo 2 could have significant clinical applications by predicting, for example, which mutations lead to diseases and distinguishing between harmless genetic variations and those that cause serious conditions.[10] The tool may also

6 "AlphaFold," Google DeepMind, May 6, 2025, https://deepmind.google/technologies/alphafold/.

7 "Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities," Carnegie Endowment for International Peace, accessed May 9, 2025, https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en.accessed May 9, 2025, https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en.","plainCitation":""Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities," Carnegie Endowment for International Peace, accessed May 9, 2025, https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en.","noteIndex":7},"citationItems":[{"id":2022,"uris":["http://zotero.org/users/8434355/items/7UNPDK9H"],"itemData":{"id":2022,"type":"webpage","abstract":"Rapid advances in bioscience and bioengineering hold immense promise for human betterment. But as these disruptive technologies become more widely distributed, their inherently dual-use nature and susceptibility to unintended consequences could create unprecedented dangers.","container-title":"Carnegie Endowment for International Peace","language":"en","title":"Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities","title-short":"Mitigating Risks from Gene Editing and Synthetic Biology","URL":"https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en","accessed":{"date-parts":[["2025",5,9]]}}}],"schema":"https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}

8 "Mitigating Risks from Gene Editing and Synthetic Biology."their inherently dual-use nature and susceptibility to unintended consequences could create unprecedented dangers.","container-title":"Carnegie Endowment for International Peace","language":"en","title":"Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities","title-short":"Mitigating Risks from Gene Editing and Synthetic Biology","URL":"https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en" ,"accessed":{"date-parts":[["2025",5,9]]}}}],"schema":"https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}

9 "Generative AI Tool Marks a Milestone in Biology | Stanford Report," accessed May 9, 2025, https://news.stanford.edu/stories/2025/02/generative-ai-tool-marks-a-milestone-in-biology-and-accelerates-the-future-of-life-sciences.

10 "Generative AI Tool Marks a Milestone in Biology | Stanford Report."

enable researchers to design entirely new genetic sequences with specific desired functions, which could revolutionize the development of new therapeutics.[11]

However, the same tools that enable breakthrough therapies could also erode the barriers to creating dangerous biological agents. A 2023 publication tells the story of researchers who modified their AI drug design system MegaSyn, so it was rewarded, instead of penalized for creating toxic components.[12] Within just a few hours, the model generated thousands of chemical warfare agents, including VX, one of the most toxic chemical agents developed for military use during the 20th century.[13] This case clearly demonstrates how quickly beneficial technologies can be redirected toward harmful purposes. As AI systems become more capable of handling complex biological design tasks, we cannot rely on the assumption that barriers that have historically impeded bioweapons development will remain intact.

How COVID-19 Transformed Risk Perceptions

The COVID-19 pandemic has fundamentally altered how governments, scientists, and the public perceive biological threats. What began as a public health crisis quickly evolved into a complex geopolitical, scientific, and governance controversy centered on the origins of SARS-CoV-2. Some Intelligence agencies, including the CIA, now assess with low to moderate confidence that a laboratory accident may have been the source of the pandemic, a position reportedly also taken by Germany's BND intelligence service as early as 2020.[14] These assessments remain highly contested, with other agencies and scientific institutions maintaining different conclusions.[15]

Regardless of the ultimate determination of origins, these assessments have catalyzed reconsiderations of biosafety protocols and dual-use research oversight

---

11 "AI Can Now Model and Design the Genetic Code for All Domains of Life with Evo 2 | Arc Institute," February 19, 2025, 2, https://arcinstitute.org/news/blog/evo2.

12 Rebecca Sohn, "AI Drug Discovery Systems Might Be Repurposed to Make Chemical Weapons, Researchers Warn," Scientific American, accessed May 9, 2025, https://www.scientificamerican.com/article/ai-drug-discovery-systems-might-be-repurposed-to-make-chemical-weapons-researchers-warn/.

13 Fabio Urbina et al., "Dual Use of Artificial Intelligence-Powered Drug Discovery," Nature Machine Intelligence 4, no. 3 (March 2022): 189–91, https://doi.org/10.1038/s42256-022-00465-9.

14 "Pandemie-Ursprung: Hielt das Kanzleramt BND-Einschätzung zu Corona zurück?," tagesschau.de, accessed May 9, 2025, https://www.tagesschau.de/inland/bnd-corona-ursprung-wuhan-labor-bundesregierung-100.html; "Covid-19: CIA Says Lab Leak Most Likely Source of Outbreak," January 26, 2025, https://www.bbc.com/news/articles/cd9qjjj4zy5o.

15 Smriti Mallapaty, "COVID Pandemic Started in Wuhan Market Animals after All, Suggests Latest Study," Nature 634, no. 8032 (September 20, 2024): 14–15, https://doi.org/10.1038/d41586-024-03026-9; Carl Zimmer, "Genetic Study Retraces the Origins of Coronaviruses in Bats," The New York Times, May 7, 2025, sec. Science, https://www.nytimes.com/2025/05/07/science/covid-coronavirus-bats-genetics.html.

frameworks.[16] As the debate has moved from technical scientific publications into mainstream discourse, it has elevated fundamental questions about the acceptable balance between scientific autonomy and public accountability. The pandemic revealed that what scientists once treated as purely technical matters of risk assessment must now contend with broader public concerns about transparency, accountability, and the moral dimensions of dual-use research. This transformation in risk perception has profound implications for how we should approach biosecurity governance in the post-COVID era.

Geopolitical Considerations

In addition to risks arising from accidental or deliberate misuse of biological agents, there is a significant strategic risk that arises from the global race for biotechnology dominance. As the National Security Commission on Emerging Biotechnology warns in its recent report, dependence on foreign biotechnology breakthroughs creates strategic vulnerabilities.[17] The report gives the example of a hypothetical revolutionary medical treatment being withheld during international tensions, forcing the government to make difficult choices between public health and geopolitical objectives.

These concerns are not merely theoretical. "The Commission has every reason to believe that the CCP will weaponize biotechnology. China already deploys genomic surveillance to identify, track, and control Uyghur Muslims, part of an extensive system of technology enabled genocide," notes the NSCEB report.[18] This assessment is reinforced by China's systematic integration of biotechnology into its Military-Civil Fusion strategy. PRC military scientists consistently emphasize biotechnology as a field that could dominate the next revolution in military affairs, with active research spanning CRISPR, bionic robotics, human enhancement technologies, and human-machine collaboration.[19]

Nations that fall behind risk critical dependencies in healthcare, materials science, and defense. The United States should strengthen domestic biotechnology

16 Executive Orders, "Improving the Safety and Security of Biological Research," The White House, May 5, 2025, https://www.whitehouse.gov/presidential-actions/2025/05/improving-the-safety-and-security-of-biological-research/.

17 "NSCEB-Full-Report---Digital--4.28.Pdf."

18 "NSCEB-Full-Report---Digital--4.28.Pdf"; "China Uses DNA to Track Its People, With the Help of American Expertise - The New York Times," accessed May 9, 2025, https://www.nytimes.com/2019/02/21/business/china-xinjiang-uighur-dna-thermo-fisher.html.

19 "China's Military Biotech Frontier: CRISPR, Military-Civil Fusion, and the New Revolution in Military Affairs," accessed May 9, 2025, https://jamestown.org/program/chinas-military-biotech-frontier-crispr-military-civil-fusion-and-the-new-revolution-in-military-affairs/.

capabilities while simultaneously developing international governance frameworks that establish responsible norms without undermining the scientific openness that has historically driven biotechnology innovation.

The Way Forward: A Technical Approach to Biosecurity

The convergence of these factors—the transformative potential of biotechnologies, their inherent dual-use nature, accelerating technical capabilities, changing risk perceptions post-COVID, and geopolitical considerations—creates both urgency and the opportunity for action. Rather than restricting innovation or establishing additional bureaucratic barriers, the United States should develop targeted technical solutions that address specific vulnerabilities while enabling continued scientific progress. A technology-centric approach offers a promising path forward by creating tools that enhance security and establish US leadership standards. The following three technical recommendations represent high-impact interventions that would fundamentally strengthen America's biodefense capabilities against both natural and engineered biological threats.

Three Technical Interventions for 21st Century Biosecurity

An adequate defense against biological threats requires an interlinked and multidisciplinary web of interventions that address vulnerabilities across the entire lifecycle of biological threats. The following three technical recommendations represent strategic points of leverage where targeted investments would yield disproportionate security benefits. These technologies address some of the most critical gaps in the US biosecurity infrastructure: safeguards for nucleic acid synthesis technologies, early detection for emerging biothreats, and reliable attribution capabilities to determine the source of biological events.

Recommendation 1: Enhance DNA Synthesis Screening and Verification

Current Challenge

Synthetic DNA has become an essential tool for biotechnology innovation, enabling breakthroughs in medicine, agriculture, and materials science.[20] Today, researchers can conveniently order DNA and RNA sequences online from commercial suppliers. As an essential resource for biological research, synthetic DNA provides a natural checkpoint to implement safeguards.

Historically, safeguarding DNA synthesis has predominantly relied on industry-led voluntary screening.[21] While significant progress towards securing this technology was made with the 2024 Framework for Nucleic Acid Synthesis Screening, significant gaps remain.[22] The recent Executive Order on Improving the Safety and Security of Biological Research calls for a revision of the 2024 framework, such as expanding oversight from only federally funded research to include non-federally funded settings.[23] This revision process provides a critical opportunity to address oversight gaps.

Closing these gaps promptly is crucial because emerging technologies are likely to introduce new vulnerabilities in current screening systems. AI-assisted protein engineering may soon enable the creation of synthetic homologs of dangerous proteins with low sequence identity to wild-type versions, potentially allowing

20 "Common-Mechanism-for-DNA-Synthesis-Screening.Pdf," accessed May 9, 2025, https://www.nti.org/wp-content/uploads/2022/11/Common-Mechanism-for-DNA-Synthesis-Screening.pdf.

21 "Preventing the Misuse of DNA Synthesis Technology," The Nuclear Threat Initiative (blog), August 3, 2023, https://www.nti.org/about/programs-projects/project/preventing-the-misuse-of-dna-synthesis-technology/.

22 "OSTP-Nucleic-Acid-Synthesis-Screening-Framework-Sep2024.Pdf," accessed June 18, 2025, https://aspr.hhs.gov/S3/Documents/OSTP-Nucleic-Acid-Synthesis-Screening-Framework-Sep2024.pdf.

23 Executive Orders, "Improving the Safety and Security of Biological Research," The White House, May 5, 2025, https://www.whitehouse.gov/presidential-actions/2025/05/improving-the-safety-and-security-of-biological-research/.

them to evade traditional detection methods.[24] Recent advances in benchtop DNA synthesizers will soon enable researchers to produce genetic material directly in their laboratories more easily, bypassing commercial providers who traditionally performed security screening.[25] Additionally, malicious actors could exploit the fragmented nature of the DNA synthesis market by splitting dangerous sequences across multiple providers to avoid detection, as current screening systems lack mechanisms to identify such coordinated ordering patterns reliably across the industry.[26]

Concerns about misapplications of technologies are not just hypothetical. The demonstration by University of Alberta researchers, who recreated an extinct relative of smallpox by assembling mail-order DNA fragments for just $100,000 without triggering security interventions, illustrates these growing risks.[27]

Recommended Actions

The United States Government should improve guardrails for synthetic DNA technologies through the following measures:

1. **Extend Mandatory Screening Beyond Federal Research**: Expand the 2024 Framework for Nucleic Acid Synthesis Screening to cover all DNA synthesis procurement, not just federally funded research. These regulations should mandate universal screening for sequences of concern, customer verification procedures, suspicious order reporting, and cybersecurity safeguards with enforcement mechanisms and penalties for non-compliance. The administration should review which existing legal authorities could support such regulations and develop a legislative proposal if further authorities are necessary.

24 Bruce J. Wittmann et al., "Toward AI-Resilient Screening of Nucleic Acid Synthesis Orders: Process, Results, and Recommendations" (bioRxiv, December 4, 2024), https://doi.org/10.1101/2024.12.02.626439.these new capabilities are creating potential biosecurity challenges by providing new pathways to intentional or accidental synthesis of genes that encode hazardous proteins. The synthesis of nucleic acids is a key choke point in the AI-assisted protein engineering pipeline as it is where digital designs are transformed into physical instructions that can produce potentially harmful proteins. Thus, one focus for efforts to enhance biosecurity in the face of new AI-enabled capabilities is on bolstering the screening of orders by nucleic acid synthesis providers. We describe a multistakeholder, cross-sector effort to address biosecurity challenges with uses of AI-powered biological design tools to reformulate naturally occurring proteins of concern to create synthetic homologs that have low sequence identity to the wild-type proteins. We evaluated the abilities of traditional nucleic acid biosecurity screening tools to detect these synthetic homologs and found that, of tools tested, not all could previously detect such AI-redesigned sequences reliably. However, as we report, patches were built and deployed to improve detection rates over the course of the project, resulting in a final mean detection rate over tools of 97% of the synthetic homologs that were determined, using in-silico metrics, to be more likely to retain wild-type-like function. Finally, we make recommendations on approaches for studying and addressing the rising risk of adversarial AI-assisted protein engineering attacks like the one we identified and worked to mitigate.","DOI":"10.1101/2024.12.02.626439","language":"en","license":"© 2024, Posted by Cold Spring Harbor Laboratory. This pre-print is available under a Creative Commons License (Attribution-NonCommercial-NoDerivs 4.0 International

25 "NTIBIO_Benchtop-DNA-Report_FINAL.Pdf," accessed May 9, 2025, https://www.nti.org/wp-content/uploads/2023/05/NTIBIO_Benchtop-DNA-Report_FINAL.pdf.

26 Forrest W. Crawford et al., "Securing Commercial Nucleic Acid Synthesis," July 1, 2024, https://www.rand.org/pubs/research_reports/RRA3329-1.html.

27 Emily Baumgaertner, "As D.I.Y. Gene Editing Gains Popularity, 'Someone Is Going to Get Hurt,'" The New York Times, May 14, 2018, sec. Science, https://www.nytimes.com/2018/05/14/science/biohackers-gene-editing-virus.html.

2. **Establish a Centralized DNA Synthesis Order Database**: Create a third-party database system that allows providers to log synthetic nucleic acid orders and identify suspicious activity patterns. This system should require providers to submit customer verification data and order disposition information using persistent identifiers.[28] It should enable the detection of split orders across multiple providers, identity fraud, and repeat attempts by previously rejected customers. The database should securely store encrypted data with appropriate privacy protections and conduct periodic retroactive screening as new sequences of concern are identified and new analytical techniques are developed.[29]

3. **Strengthen Screening Against AI-Assisted Evasion Techniques:** Update current screening methods to improve effectiveness in detecting modified sequences of concern. Given protein design tools' potential misapplication to avoid traditional screening techniques, the US government should regularly review, test, and update existing screening methods to account for this evolving risk.

Expected Outcomes

This narrowly-targeted approach would substantially reduce the risk of dangerous sequences being synthesized without appropriate oversight, while avoiding the introduction of unnecessary barriers to legitimate research. By establishing this framework domestically, the US would also set a global standard that other countries could adopt, potentially prompting similar regulations internationally through America's position as a bioeconomy leader.

Economic and Innovation Benefits

To avoid hindering innovation, this framework should be designed with input from industry stakeholders to minimize regulatory burden while maximizing security benefits. Clear regulatory guidance for the synthetic biology industry will enable confident investment and growth. US leadership in biosecurity standards would position American companies advantageously in the global market, creating opportunities for technology development and export of screening solutions.

28 Crawford et al., "Securing Commercial Nucleic Acid Synthesis."

29 Crawford et al.

Recommendation 2: Develop Advanced Pathogen Early Warning Systems

Current Challenge

Early warning systems are a cornerstone of strong preparedness, yet current systems often identify biological threats days, weeks, or even months after they emerge, providing dangerous windows for infectious diseases to spread.[30] This delay is particularly concerning for pathogens with pre-symptomatic or asymptomatic transmission. Many diagnostic tools also focus on specific, known diseases rather than searching for a broader range of biological threats, leaving critical blind spots for novel emerging threats. Across the United States and globally, surveillance capabilities are fragmented and inconsistent, with outdated technologies, poor training, and inefficient systems that fail to characterize and respond to disease threats in a timely manner.[31]

Despite significant financial commitment, with approximately $700 million allocated to pathogen detection across federal agencies in 2019, the COVID-19 pandemic revealed fundamental weaknesses in the US biosurveillance infrastructure.[32] Real-time, reliable infection data remained elusive during crucial early pandemic stages. However, some investments did prove their value during the crisis. When a Cooperative Threat Reduction (CTR) program-supported laboratory in Thailand became the first facility outside of China to detect COVID-19, it exemplified how international biological defense networks can provide essential early warning of threats that might otherwise reach the United States undetected.[33]

The current system continues to suffer from institutional fragmentation, with responsibilities scattered across numerous departments, including the Department of Health and Human Services (HHS), the Department of Defense (DoD), the

30 Dr Natasha E Bajema, William Beaver, and Christine Parthemore, "BUILDING ON THE LANDSCAPE OF BIOSURVEILLANCE TODAY," n.d.

31 Bajema, Beaver, and Parthemore.

32 "Mapping America's Biosurveillance | IFP," April 3, 2024, https://ifp.org/mapping-americas-biosurveillance/.

33 Jess Rogers, "America Will Regret DOGE's Cuts to Our Nuclear Security," The National Interest (blog), accessed June 18, 2025, https://nationalinterest.org/feature/america-will-regret-doges-cuts-to-our-nuclear-security.

Department of Homeland Security (DHS), and the Department of Energy, often with minimal coordination between these efforts.[34]

Recommended Actions

The United States, in coordination with partners, should establish a comprehensive early warning system through targeted technological investments:

1. **Accelerate Advanced Detection Technology Development**: Increase R&D funding for comprehensive pathogen detection technologies, including metagenomic sequencing, CRISPR-based diagnostics, and environmental monitoring systems. Pathogen-agnostic capabilities, which can detect all pathogens, including previously unknown ones, should be prioritized for strategic deployment at critical high-risk locations, such as areas with high zoonotic spillover potential and urban centers. ARPA-H should establish a dedicated program to overcome current sample processing bottlenecks by developing faster and cheaper technologies that prepare heterogeneous clinical samples for sequencing.[35]

2. **Enhance CDC Surveillance Programs**: Leverage CDC's existing National Wastewater Surveillance System (NWSS) and Traveler-based Genomic Surveillance (TGS) Program by establishing public-private partnerships to conduct regular metagenomic sequencing on collected samples.[36] After de-identification, the resulting sequencing data should be made accessible in real-time for analysis by the broader scientific and public health community.[37]

34 "Mapping America's Biosurveillance | IFP," April 3, 2024.

35 "Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook," Techno-Industrial Policy Playbook, accessed June 18, 2025, https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing.2025, https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing.","plainCitation":""Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook," Techno-Industrial Policy Playbook, accessed June 18, 2025, https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing.","noteIndex":35},"citationItems":[{"id":2119,"uris":["http://zotero.org/users/8434355/items/VAH8U6NC"],"itemData":{"id":2119,"type":"webpage","abstract":"Enhancing US biosurveillance through the adoption of metagenomic sequencing.","container-title":"Techno-Industrial Policy Playbook","language":"en","title":"Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook","URL":"https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing","accessed":{"date-parts":[["2025",6,18]]}}}],"schema":"https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}

36 "Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook.""container-title":"Techno-Industrial Policy Playbook","language":"en","title":"Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook","URL":"https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing","accessed":{"date-parts":[["2025",6,18]]}}}],"schema":"https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}

37 "Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook.""container-title":"Techno-Industrial Policy Playbook","language":"en","title":"Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook","URL":"https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing","accessed":{"date-parts":[["2025",6,18]]}}}],"schema":"https://github.com/citation-style-language/schema/raw/master/csl-citation.json"}

3. **Create a Unified National Surveillance Framework:** Develop and test an integrated biological surveillance system (BioRadar) designed to detect and attribute emerging biological threats, including biological weapons, while protecting individual privacy and enabling rapid public health response. As the first step towards building a national system, develop proof-of-concept pilot programs in select cities to build prototype BioRadar systems that characterize baseline biological profiles of communities, enabling rapid detection and examination of deviations and perturbations.

Expected Outcomes

This comprehensive early warning system could dramatically reduce the time between a pathogen's emergence and its detection, potentially from weeks to hours in many scenarios. By combining environmental surveillance with advanced analytics, the system would be capable of detecting both known and novel biological threats before they become widespread. This capability would provide critical time for containment measures, potentially preventing localized outbreaks from becoming national or global emergencies.

Economic and Innovation Benefits

Investment in these technologies could create new markets for biosurveillance products and position American companies as global leaders in this emerging sector. By reducing vulnerability to biological disruptions, these systems would provide economic security by helping prevent future pandemic-scale events that could cost trillions in economic damage. Additionally, these capabilities would strengthen America's biodefense posture, acting as a potential deterrent for bioterrorist attacks.

Recommendation 3: Improve Genetic Engineering Detection and Attribution Capabilities

Current Challenge

The ongoing debate surrounding the origins of COVID-19 and the lab leak hypothesis has highlighted a critical vulnerability in the US biosecurity infrastructure: the limited ability to determine the source of biological agents with high confidence. Whether COVID-19 ultimately proves to be natural in origin or the result of a laboratory incident, the controversy has revealed how difficult it is to establish attribution in biological events. This uncertainty has undermined public trust, complicated international relations, and left policymakers without clear answers on how to respond.

However, research suggests that reliable attribution may be technically feasible. Researchers have shown that the design choices made by genetic engineers create distinct "methodological signatures" that can be traced back to their creators with up to 81.9% accuracy when distinguishing between different laboratories.[38]

Attribution has three main security benefits in the context of biological events:

1. **Intelligence:** Knowledge of who was responsible can inform response efforts by shedding light on motives and capabilities, allowing authorities to mitigate the event's consequences more effectively.
2. **Accountability:** Attribution can identify the responsible parties for appropriate civil, criminal, or diplomatic penalties.

38 Oliver M. Crook et al., "Analysis of the First Genetic Engineering Attribution Challenge," Nature Communications 13, no. 1 (November 30, 2022): 7374, https://doi.org/10.1038/s41467-022-35032-8.while holding designers accountable to the communities they affect. Here, we present the results of the first Genetic Engineering Attribution Challenge, a public data-science competition to advance GEA techniques. Top-scoring teams dramatically outperformed previous models at identifying the true lab-of-origin of engineered plasmid sequences, including an increase in top-1 and top-10 accuracy of 10 percentage points. A simple ensemble of prizewinning models further increased performance. New metrics, designed to assess a model's ability to confidently exclude candidate labs, also showed major improvements, especially for the ensemble. Most winning teams adopted CNN-based machine-learning approaches; however, one team achieved very high accuracy with an extremely fast neural-network-free approach. Future work, including future competitions, should further explore a wide diversity of approaches for bringing GEA technology into practical use.","container-title":"Nature Communications","DOI":"10.1038/s41467-022-35032-8","ISSN":"2041-1723","issue":"1","journalAbbreviation":"Nat Commun","language":"en","license":"2022 The Author(s

3. **Deterrence:** Successful attribution, followed by meaningful actions to hold perpetrators accountable, can deter those inclined to reckless or malicious practices in the first place.[39]

Recommended Actions

The United States should establish national genetic engineering detection and attribution capabilities through the following measures:

1. **Create a National Biodefense Attribution Plan**: Develop a comprehensive, whole-of-government strategy for bioattribution that delineates clear roles and responsibilities among key agencies, including DHS, DoD, DoS, HHS, FBI, and the Department of the Interior—for both domestic and international events.[40] This plan should establish coordination mechanisms, formalize information-sharing protocols between agencies, and provide a timeline for implementing next-generation attribution capabilities.[41]

2. **Develop Comprehensive Training Datasets and Detection Systems**: Build robust attribution capabilities by creating more diverse training datasets and including data from a broader range of laboratories across multiple countries and regions. These systems must be designed to identify clandestine laboratories not present in training data through inference of regional and methodological characteristics.

3. **Establish Adversary-Resistant Attribution Technologies**: Develop advanced forensic capabilities that can reliably detect genetic engineering signatures even when actors attempt to obfuscate their methods through AI-assisted signature masking or other evasion techniques. Attribution algorithms must be designed with robustness against such obfuscation attempts, ensuring reliable detection despite adversarial efforts to conceal laboratory origins.

39 Gregory Lewis et al., "The Biosecurity Benefits of Genetic Engineering Attribution," Nature Communications 11, no. 1 (December 8, 2020): 6294, https://doi.org/10.1038/s41467-020-19149-2.and the risk of this causing widespread harm increases in step with the rapid march of technological progress. A key security challenge involves attribution: determining, in the wake of a human-caused biological event, who was responsible. Recent scientific developments have demonstrated a capability for detecting whether an organism involved in such an event has been genetically modified and, if modified, to infer from its genetic sequence its likely lab of origin. We believe this technique could be developed into powerful forensic tools to aid the attribution of outbreaks caused by genetically engineered pathogens, and thus protect against the potential misuse of synthetic biology.","container-title":"Nature Communications","DOI":"10.1038/s41467-020-19149-2","ISSN":"2041-1723","issue":"1","journalAbbreviation":"Nat Commun","language":"en","license":"2020 The Author(s

40 "Mapping America's Biosurveillance | IFP," April 3, 2024, https://ifp.org/mapping-americas-biosurveillance/.

41 "Mapping America's Biosurveillance | IFP."

Expected Outcomes

These detection and attribution capabilities would strengthen national security by providing critical intelligence on whether an organism has been engineered, enabling more effective response strategies tailored to the specific threat. By establishing technical means to identify responsible parties, the system would create meaningful accountability through appropriate legal, diplomatic, or security responses. Perhaps most importantly, the existence of reliable attribution technologies backed by consequential enforcement mechanisms would serve as a powerful deterrent against reckless or malicious biological activities, fundamentally changing risk calculations for bad actors.

Economic and Innovation Benefits

Investment in these technologies would accelerate advances in genomic analysis, bioinformatics, and computational biology with applications beyond security. he technical capabilities developed could have commercial applications in intellectual property protection for engineered organisms, quality control for synthetic biology companies, and verification for biological manufacturing. By leading in this field, the US would establish both security advantages and economic benefits in the growing bioeconomy.

Conclusion

Implementing these three recommendations—improvements in DNA synthesis screening, pathogen early warning systems, and genetic engineering detection and attribution capabilities—will provide a much-needed enhancement of the US's capabilities to prevent, detect, and respond to biothreats.

These complementary technologies create a robust multi-layered security approach: screening makes it harder to synthesize dangerous sequences, early warning systems detect threats before they spread widely, and attribution capabilities ensure accountability while deterring reckless or malicious actions. Together, they form a layered technical defense that balances innovation with security, addressing the dual-use dilemma while positioning the United States at the forefront of the rapidly expanding biotechnology frontier.

The devastating impact of COVID-19 on American lives and the economy serves as a stark reminder of our vulnerability to biological threats. The investments required to implement these three technical recommendations represent a modest commitment compared to the scale of future risks they could help prevent. By acting decisively now to develop and deploy these technologies, the United States can protect its citizens, strengthen its economy, and establish global leadership in addressing one of the most significant security challenges of the 21st century.

References

"AI Can Now Model and Design the Genetic Code for All Domains of Life with Evo 2 | Arc Institute," February 19, 2025. https://arcinstitute.org/news/blog/evo2.

Bajema, Dr Natasha E, William Beaver, and Christine Parthemore. "BUILDING ON THE LANDSCAPE OF BIOSURVEILLANCE TODAY," n.d.

Baumgaertner, Emily. "As D.I.Y. Gene Editing Gains Popularity, 'Someone Is Going to Get Hurt.'" *The New York Times*, May 14, 2018, sec. Science. https://www.nytimes.com/2018/05/14/science/biohackers-gene-editing-virus.html.

BCG Global. "Synthetic Biology Is About to Disrupt Your Industry," February 8, 2022. https://www.bcg.com/publications/2022/synthetic-biology-is-about-to-disrupt-your-industry.

"CAR T Cell Therapy: A Remarkable Breakthrough in Cancer Treatment." Accessed May 9, 2025. https://www.wolterskluwer.com/en/expert-insights/car-t-cell-therapy-a-remarkable-breakthrough-in-cancer-treatment.

Carnegie Endowment for International Peace. "Mitigating Risks from Gene Editing and Synthetic Biology: Global Governance Priorities." Accessed May 9, 2025. https://carnegieendowment.org/research/2024/10/mitigating-risks-from-gene-editing-and-synthetic-biology-global-governance-priorities?lang=en.

"China Uses DNA to Track Its People, With the Help of American Expertise - The New York Times." Accessed May 9, 2025. https://www.nytimes.com/2019/02/21/business/china-xinjiang-uighur-dna-thermo-fisher.html.

"China's Military Biotech Frontier: CRISPR, Military-Civil Fusion, and the New Revolution in Military Affairs." Accessed May 9, 2025. https://jamestown.org/program/chinas-military-biotech-frontier-crispr-military-civil-fusion-and-the-new-revolution-in-military-affairs/.

Commissioner, Office of the. "FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease." FDA. FDA, September 8, 2024. https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.

"Common-Mechanism-for-DNA-Synthesis-Screening.Pdf." Accessed May 9, 2025. https://www.nti.org/wp-content/uploads/2022/11/Common-Mechanism-for-DNA-Synthesis-Screening.pdf.

"Covid-19: CIA Says Lab Leak Most Likely Source of Outbreak," January 26, 2025. https://www.bbc.com/news/articles/cd9qjjj4zy5o.

Crawford, Forrest W., Kyle Webster, Gerald L. Epstein, Derek Roberts, Joseph Fair, and Sella Nevo. "Securing Commercial Nucleic Acid Synthesis," July 1, 2024. https://www.rand.org/pubs/research_reports/RRA3329-1.html.

Crook, Oliver M., Kelsey Lane Warmbrod, Greg Lipstein, Christine Chung, Christopher W. Bakerlee, T. Greg McKelvey, Shelly R. Holland, et al. "Analysis of the First Genetic Engineering Attribution Challenge." *Nature Communications* 13, no. 1 (November 30, 2022): 7374. https://doi.org/10.1038/s41467-022-35032-8.

"Generative AI Tool Marks a Milestone in Biology | Stanford Report." Accessed May 9, 2025. https://news.stanford.edu/stories/2025/02/generative-ai-tool-marks-a-milestone-in-biology-and-accelerates-the-future-of-life-sciences.

Google DeepMind. "AlphaFold," May 6, 2025. https://deepmind.google/technologies/alphafold/.

Lewis, Gregory, Jacob L. Jordan, David A. Relman, Gregory D. Koblentz, Jade Leung, Allan Dafoe, Cassidy Nelson, et al. "The Biosecurity Benefits of Genetic Engineering Attribution." *Nature Communications* 11, no. 1 (December 8, 2020): 6294. https://doi.org/10.1038/s41467-020-19149-2.

Mallapaty, Smriti. "COVID Pandemic Started in Wuhan Market Animals after All, Suggests Latest Study." *Nature* 634, no. 8032 (September 20, 2024): 14–15. https://doi.org/10.1038/d41586-024-03026-9.

"Mapping America's Biosurveillance | IFP," April 3, 2024. https://ifp.org/mapping-americas-biosurveillance/.

"Mapping America's Biosurveillance | IFP," April 3, 2024. https://ifp.org/mapping-americas-biosurveillance/.

Naidoo, Kubendran, and Shüné V. Oliver. "Gene Drives: An Alternative Approach to Malaria Control?" *Gene Therapy* 32, no. 1 (January 2025): 25–37. https://doi.org/10.1038/s41434-024-00468-8.

"NSCEB-Full-Report-–-Digital-–4.28.Pdf." Accessed May 9, 2025. https://www.biotech.senate.gov/wp-content/uploads/2025/04/NSCEB-Full-Report-%E2%80%93-Digital-%E2%80%934.28.pdf.

"NTIBIO_Benchtop-DNA-Report_FINAL.Pdf." Accessed May 9, 2025. https://www.nti.org/wp-content/uploads/2023/05/NTIBIO_Benchtop-DNA-Report_FINAL.pdf.

Orders, Executive. "Improving the Safety and Security of Biological Research." The White House, May 5, 2025. https://www.whitehouse.gov/presidential-actions/2025/05/improving-the-safety-and-security-of-biological-research/.

———. "Improving the Safety and Security of Biological Research." The White House, May 5, 2025. https://www.whitehouse.gov/presidential-actions/2025/05/improving-the-safety-and-security-of-biological-research/.

"OSTP-Nucleic-Acid-Synthesis-Screening-Framework-Sep2024.Pdf." Accessed June 18, 2025. https://aspr.hhs.gov/S3/Documents/OSTP-Nucleic-Acid-Synthesis-Screening-Framework-Sep2024.pdf.

"Postpn340.Pdf." Accessed May 9, 2025. https://www.parliament.uk/globalassets/documents/post/postpn340.pdf.

Rogers, Jess. "America Will Regret DOGE's Cuts to Our Nuclear Security." *The National Interest* (blog). Accessed June 18, 2025. https://nationalinterest.org/feature/america-will-regret-doges-cuts-to-our-nuclear-security.

Sohn, Rebecca. "AI Drug Discovery Systems Might Be Repurposed to Make Chemical Weapons, Researchers Warn." Scientific American. Accessed May 9, 2025. https://www.scientificamerican.com/article/ai-drug-discovery-systems-might-be-repurposed-to-make-chemical-weapons-researchers-warn/.

tagesschau.de. "Pandemie-Ursprung: Hielt das Kanzleramt BND-Einschätzung zu Corona zurück?" Accessed May 9, 2025. https://www.tagesschau.de/inland/bnd-corona-ursprung-wuhan-labor-bundesregierung-100.html.

Techno-Industrial Policy Playbook. "Accelerating the Defensive Deployment of Pathogen Sequencing | The Techno-Industrial Policy Playbook." Accessed June 18, 2025. https://www.rebuilding.tech/posts/accelerating-the-defensive-deployment-of-pathogen-sequencing.

The Nuclear Threat Initiative. "Preventing the Misuse of DNA Synthesis Technology," August 3, 2023. https://www.nti.org/about/programs-projects/project/preventing-the-misuse-of-dna-synthesis-technology/.

Urbina, Fabio, Filippa Lentzos, Cédric Invernizzi, and Sean Ekins. "Dual Use of Artificial Intelligence-Powered Drug Discovery." *Nature Machine Intelligence* 4, no. 3 (March 2022): 189–91. https://doi.org/10.1038/s42256-022-00465-9.

Wittmann, Bruce J., Tessa Alexanian, Craig Bartling, Jacob Beal, Adam Clore, James Diggans, Kevin Flyangolts, et al. "Toward AI-Resilient Screening of Nucleic Acid Synthesis Orders: Process, Results, and Recommendations." bioRxiv, December 4, 2024. https://doi.org/10.1101/2024.12.02.626439.

Zimmer, Carl. "Genetic Study Retraces the Origins of Coronaviruses in Bats." *The New York Times,* May 7, 2025, sec. Science. https://www.nytimes.com/2025/05/07/science/covid-coronavirus-bats-genetics.html.

Belfer Center for Science and International Affairs
Harvard Kennedy School
79 JFK Street
Cambridge, MA 02138

www.belfercenter.org

HARVARD Kennedy School BELFER CENTER | 50 YEARS OF RESEARCH, POLICY, AND LEADERSHIP