A HANDBOOK FOR ENDING CATASTROPHIC BIOLOGICAL RISKS

HOW THE UNITED STATES CAN PREVENT FUTURE PANDEMICS AND DETER BIOLOGICAL WEAPONS

THE JANNE E. NOLAN CENTER ON STRATEGIC WEAPONS
AN INSTITUTE OF
THE COUNCIL ON STRATEGIC RISKS

By William Beaver, Dr. Yong-Bee Lim, Lillian Parr, Christine Parthemore, and Andrew Weber

With contributing authors Dr. Natasha Bajema, Dr. Rohit Chitale, Jackson duPont, Dr. Chris Fall, Dr. Nikki Teran, and Dr. Alexander Titus

Edited by Francesco Femia and Christine Parthemore

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AUTHORS' NOTE

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I. EXECUTIVE SUMMARY

The global devastation wrought by the COVID-19 pandemic highlights the urgent need to improve U.S. national strategy and responses to biological threats. The pandemic, which continues in force as of this writing, has shown that infectious disease threats can take millions of lives, cost trillions of dollars, imperil national security, and strain geopolitical relations in an already complex and tense global security landscape. Moreover, as terrible as the COVID-19 pandemic has been, the United States and the world could face even more destructive biological threats in the coming years.

It is unacceptable to allow this situation to continue, especially given the incredible knowledge and technology bases housed across the U.S. government, academia, and the private sector. This report, *A Handbook for Ending Catastrophic Biological Risks: How the United States Can Deter Biological Weapons and Prevent Future Pandemics,* offers a better path.

While we recognize the need for significant improvements in public health, this report is scoped to efforts focused on addressing *catastrophic biological risks* - those that may produce mass casualty events or by other mechanisms significantly change the trajectory of humanity.[1] It is also written primarily through the lens of improving U.S. government policies, programs, and investments, while recognizing that most progress toward addressing catastrophic biological risks will stem from public-private cooperation and a shared international vision. This Executive Summary proceeds with a brief overview of the shifts in U.S. national strategy the report recommends, followed by examples of how that strategy should be enacted through national plans, programs, and investments.

A STRONG VISION FOR U.S. NATIONAL STRATEGY

Creating a new future where the United States aggressively addresses catastrophic biological risks and maintains this work as a high priority will require several key elements. The most important is a bold, moonshot-level vision that inspires people and creates political momentum for increasing resources. Such a vision must be clear and compelling, and it must be big enough to drive transformative changes---not the incremental improvements the U.S. government has often pursued in the past.

In terms of naturally-arising biological risks, the United States is already beginning to embrace an ideal vision: *preventing future pandemics.* With the expansion of robust early warning capacities, rapid responses, and improved international coordination, the nation's aim should be to stop outbreaks from growing to pandemic scale---not simply enduring them and accepting the lives lost and damage to health security, national security, and the economy that pandemics can cause.

1 Monica Schoch-Spana, Anita Cicero, Amesh Adalja, Gigi Gronvall, Tara Kirk Sell, Diane Meyer, Jennifer B. Nuzzo, Sanjana Ravi, Matthew P. Shearer, Eric Toner, Crystal Watson, Matthew Watson, and Tom Inglesby, "Global Catastrophic Biological Risks: Toward a Working Definition," *Health Security* Vol. 15, No. 4, 2017: pp. 323 - 328.

This report recommends continued, strong progress toward the vision of preventing future pandemics. It also recommends a complementary, robust U.S. strategy to deter deliberate biological threats, one which will require far more significant shifts in the nation's goals and policies. It therefore proposes that U.S. leaders set the following vision for the nation:

> *The United States should lead the world in making biological weapons the first category of weapons of mass destruction to be effectively eliminated or rendered obsolete.*

To advance this vision, the report recommends that national security leaders adopt a "deterrence by denial" strategy that focuses on denying an attacker success in their likely aims regarding biological weapons, such as causing mass casualties, mass confusion, and erosion of operational capabilities. This would both mark several major policy changes for the United States and significantly improve how U.S. federal agencies leverage the innovation occurring across the nation. As this shift in the nation's approach would require more changes from its current path than is the case for pandemic prevention, it is the focus of much of this handbook.

IMPLEMENTING AN AMBITIOUS VISION

Some of the changes that implementing these goals will require in U.S. policies, programs, and investments are already underway. The nation is beginning to create a system for addressing biological risks far more effectively. This is due to both decades of innovation, and the acceleration of game-changing technologies in response to the COVID-19 pandemic. Still, several shifts in the U.S. approach to addressing catastrophic biological risks are warranted, as described throughout this report.

Ensure an All Hands on Deck Approach. The United States needs an approach for addressing biological risks that maximizes and coordinates all of the nation's top assets. In addition to the crucial programs run by the Department of Health and Human Services, game-changing contributions by the Departments of Defense and Energy, for example, are not as well recognized. Future changes to U.S. national strategy in this area must set an "all hands on deck" approach that recognizes the full range of personnel and technological assets the nation has, unites them, and ensures strong investments in their continuing innovation.

Take a Systemic Approach to a Strong Bio-Industrial Base. No single aspect of pandemic prevention or deterring biological weapons activities is sufficient. Rather, an interoperable system is required that includes robust early warning, strong diagnostic tools that capture wide-ranging pathogen threats, and the capacity to rapidly develop new medical countermeasures and get them into use, among other steps. Further, an effective system will require diverse and geographically-dispersed tools and technologies that may necessitate more creative approaches to federal contracting and support to additional cutting-edge labs and companies. The United States also needs to foster a strong manufacturing base to support this systemic approach to mitigating biological threats, and test it via an annual exercise program that identifies areas for continual improvement.

Sustain and Build on Improvements Made for COVID-19 Responses. Despite the nation's struggles in responding to the COVID-19 pandemic, many advancements have been made. The capacities the nation is developing for COVID-19 testing, therapeutic and vaccine development and manufacturing,

and pathogen early warning must be sustained as the new baseline on which the nation continues to build. There can be no reverting back to pre-pandemic conditions.

Drive Change through Robust International Cooperation. This handbook focuses on U.S. policies and investments, though the initiatives it recommends can apply to many nations. Moreover, U.S. success in ending catastrophic biological risks will only be possible with robust international cooperation. The United States should pursue a surge in diplomacy, outreach, global technology-sharing, and threat reduction cooperation as a key component in future efforts to mitigate and actively address these threats.

Building on these broad themes, this report contains dozens of recommendations, most pertaining to specific agencies. The following table provides relevant snapshots on the current state of play for major U.S. departments, along with key examples of this report's recommendations for implementing a more effective strategy.

Work to address biological threats has long been subject to cycles of neglect, which has had grave consequences. The COVID-19 pandemic makes clear that this has proven far more costly than robust, consistent resourcing. In order to align investments to implement the vision outlined in this report, we propose that the U.S. federal government adopt a resourcing plan that we call 10+10 over 10: investments of $10 billion per year for ten years for deterring and addressing biological weapons threats, plus $10 billion per year for ten years for global health security and direct pandemic prevention initiatives. Of course, resources in each category contribute to the objectives of the other. Together they can ensure that pivotal work is conducted to bring an end to catastrophic biological risks before they cause mass devastation and destruction.

TABLE 1: STATE OF PLAY AND RECOMMENDED U.S. STEPS TO END CATASTROPHIC BIOLOGICAL RISKS

AGENCY	STATE OF PLAY	ELEMENTS OF A MORE EFFECTIVE STRATEGY
Department of Defense (DoD) *Key entities include the Chemical and Biological Defense Program (CBDP), the Biological Threat Reduction Program (BTRP), the Defense Advanced Research Projects Agency (DARPA), & the United States Army Medical Research Institute of Infectious Diseases (USAMRIID)*	-Plays a central role in addressing biological threats & holds unique authorities and talent - Resources have been diverted for years and programs remain under-invested - Biodefense and the missions of specific programs are too narrowly defined - The current strategic vision leaves vulnerabilities and accepts too much risk	- Develop & implement a "deterrence by denial" strategy regarding biological weapons threats - Expand missions of key programs to include deterrence - Leverage DoD assets against the full range of significant biological risks of any origin - Improve use of DoD laboratories for early warning and response - Implement an annual exercise program to enhance early warning & rapid response capabilities - Expand the CBDP significantly - Use the BTRP to deploy new technologies for pathogen early warning - Revamp DARPA's Biological Technologies Office to better suit conducting biological research useful for meeting national security goals - Broaden the mission of USAMRIID & grant the institute more independence through restructuring - Continue focus on pathogen-agnostic, flexible tools and platforms
Department of Health and Human Services (HHS) *Key entities include the Office of the Assistant Secretary for Preparedness and Response (ASPR), Biomedical Advanced Research and Development Authority (BARDA), & the National Institutes of Health (NIH)*	-HHS programs are integral to addressing biological threats & played a central role in innovation to respond to COVID-19 -ASPR and BARDA are gaining new resources and have strong programs hastening innovation - NIH conducts basic and applied health-related research & receives more than 1/3 of government R&D spending on biological threats -The CDC and FDA are also crucial, with broader mandates than the focus of this report	- Re-envision the Strategic National Stockpile as an asset for a healthy bio-industrial base and rapid response to crises - Expand programs that have shown incredible value during COVID-19, such as RADx - Launch ARPA-H and ensure a strong focus on infectious disease threats - Expand interagency collaboration for better transitioning early stage research into development and procurement - Set data standards for improving data sharing and interoperability for pathogen early warning - Fund research with high impact potential, especially platform technologies & pathogen-agnostic tools - Provide stronger and clearer guidance on gain-of-function research - Maintain a strong partnership with the DoD

Department of State	- Plays a critical role in forging relationships with international partners to meet biosecurity goals & advance global health security - Leads engagement on the Biological Weapons Convention (BWC)	- Create new multi- and minilateral mechanisms for bio cooperation that enhance the BWC and complement existing international structures - Leverage existing and emerging technologies to enable verification of treaty compliance - Expand diplomacy on pathogen early warning - Appoint a special envoy dedicated to addressing biological threats and increase the number of staff with biorisk expertise
Department of Energy (DoE) National Laboratories	- Conducts research & develops technology to advance national security goals - Responded to the COVID-19 pandemic with research on structural biology of the virus, epidemiological modeling & much more - Underutilized for its contributions in biosecurity	- Make DoE and the National Labs leaders in engineering biology for the nation - Create a Biosecurity Reserve Corps in which non-governmental experts sign on for a period of service & can be easily called on in crises - Rededicate the National Nuclear Security Administration (NNSA) to the biosecurity mission - Reestablish the Chemical and Biological Nonproliferation Program - Develop a permanent coordination framework that facilitates public-private interactions
Department of Homeland Security (DHS) *Key programs include the Countering Weapons of Mass Destruction Office & the Science & Technology Directorate*	- Builds infrastructure to allow information sharing across the interagency - Conducts surveillance, including through the BioWatch Program - Conducts attribution analysis through bioforensics work	- Conduct an assessment of operational and analytical processes to identify gaps - Integrate with the newly established CDC Center for Forecasting and Outbreak Analytics - Increase the efficacy and accuracy of bioforensics capabilities to aid in deterring bioweapons attacks
Interagency & Systemic Changes	- Due to advances during the COVID-19 response and changes in the technology landscape, the U.S. interagency is primed for systemic, dramatic improvements - The race to create COVID-19 medical countermeasures made clear the importance of cooperation among government agencies in reducing biological threats	- Create the role of Chief Biotechnology Officers in all key agencies - Ensure a strong medical countermeasures manufacturing base supported by various government agencies - Set guidance for early warning signals triggering medical countermeasure and diagnostics development responses - Conduct a regular exercise program to continually improve responses - Make use of rapid and flexible authorities & seek to expand them where needed - Improve transparency in spending - Prioritize recruiting & retaining talented staff

II. INTRODUCTION TO THE HANDBOOK

The world has a long history of both significant infectious disease outbreaks and pathogens being deliberately used to harm others---weaponized to undermine opposing military forces or deployed simply to sicken and undercut targeted populations. Sophistication grew around the time of the World Wars and the decades after. In 1925, world leaders saw the potential devastation of this trend and introduced the Geneva Protocol, which outlawed the "first use" of biological weapons in warfare but did not stop countries from developing them for potential retaliation if attacked with the biological weapons of others.[2]

As the world descended into the Cold War, multiple countries began experimenting with offensive biological weapons. A few developed robust programs and infrastructure, and detailed concepts for how to potentially use their bioweapons arsenals in warfare.

The Biological Weapons Convention that entered into force in 1975 (and activities leading to the treaty) led to the halting of many of these activities, though biological weapons activities have not yet fully ended. Adding to these continuing threats are significant advancements in biotechnology in recent years, which will mostly benefit humanity but may make the misuse of biology easier. In addition to these deliberate threats, the frequency of lab accidents and naturally-arising disease outbreaks is rising. In the worst case in a century, COVID-19 is continuing through its second year, having already killed several million people and sickened millions more, providing a wake-up call of the systemic-level impact of biological threats.[3]

The Council on Strategic Risks (CSR) was formed in 2017 with a mission of analyzing, anticipating, and addressing systemic threats to international security, with biological threats playing a central role in the organization's work. CSR is conducting a multi-year initiative to promote a shift to bolder and more ambitious U.S. strategies and policies for addressing biological threats. This initiative has fueled the issues and recommendations highlighted in this report.

While the United States must take on broad and urgent public health improvements, this report is scoped to efforts focused on addressing *catastrophic biological risks*. These are often defined as biological risks that could produce sudden disasters, mass casualty events, or by other means significantly change the trajectory of humanity.[4] In particular, it offers a deep-dive into the potentially catastrophic risks of biological weapons that are *designed and used with the intention of game-changing destruction*---and what to do about this threat.

CSR proposes that the United States should set a new vision of preventing future pandemics and robbing biological weapons of their ability to cause such catastrophic damage. For the latter, this would entail national leaders setting

2 The United Nations, "1925 Geneva Protocol."

3 Ibid.

4 A fuller definition is offered in Monica Schoch-Spana, Anita Cicero, Amesh Adalja, Gigi Gronvall, Tara Kirk Sell, Diane Meyer, Jennifer B. Nuzzo, Sanjana Ravi, Matthew P. Shearer, Eric Toner, Crystal Watson, Matthew Watson, and Tom Inglesby, "Global Catastrophic Biological Risks: Toward a Working Definition," *Health Security* Vol. 15, No. 4, 2017: pp. 323 - 328.

a goal of biological weapons being the first category of weapons of mass destruction to be *effectively eliminated* through robust deterrence. This can be pursued through capabilities aimed at significantly enhanced preparedness and response capacities---many of which are already being deployed today.

This report is a handbook that presents a policy roadmap for moving the nation in this direction---hopefully alongside allies and partners, and other nations around the world. It first provides a brief overview regarding biological threats in *Part III*. *Part IV* then sets this high-level vision and strategic direction for addressing these threats. *Part V* explores key U.S. agencies and programs that will contribute to implementing this improved strategy for the nation, including examples of the critical work they perform and recommendations for how they should evolve in the coming years. As many functions (such as disease tracking and countermeasure development) cross multiple government agencies, *Part VI* provides several examples of these cross-cutting functional requirements. Finally, *Part VII* is an overview of a recommended 10-year national budget in support of this updated, and likely more effective, approach to addressing catastrophic biological threats.

Throughout this report, the reader will find descriptions of the key U.S. government programs whose future will determine the pace and shape of how this vision is enacted in the years ahead. It also includes text boxes highlighting certain tools of the bureaucratic trade that will enable implementation, such as the use of rapid acquisition and flexible legal authorities and mechanisms for aligning the right personnel with supporting roles.

Within the context of the daily confusion that seems to reign in the public discourse on the current pandemic, we hope this document will serve as a handbook for U.S. officials and experts who seek a clear, viable and improved path toward addressing catastrophic biological threats---one of the most daunting risks facing the world.

Renaissance Island (Vozrozhdeniya Island), Uzbekistan and Kazakhstan. In the early 1970s, Soviet experiments with weaponized smallpox on Vozrozhdeniya Island are suspected to have led to accidental exposure of a scientific ship in the Aral Sea and several deaths. NASA

III. BIOLOGICAL THREATS

On May 4th, 2021, the U.S. House Armed Services Committee held a hearing on how the United States has addressed weapons of mass destruction (WMD) threats in the past. The hearing also covered how factors such as globalization, emerging technologies, and geopolitical shifts are potentially exacerbating the biological threats that the United States faces from state and non-state actors. Toward the end of the hearing, Subcommittee Chairman Rep. Ruben Gallego raised the alarm, stating: "...the COVID-19 pandemic has shown just how devastating biological threats can be - in this case, the novel coronavirus was not weaponized. But it could be."[5]

5 U.S. House Armed Services Committee, "20210504 ISO Hearing: 'Reviewing20210504 ISO Hearing: "Reviewing DOD Strategy, Policy, and Programs for Countering WMD in FY22" DOD Strategy, Policy, and Programs for Countering WMD in FY22,'" YouTube Video, 1:32:50, May 4, 2021.

The weaponization of disease is not new to human history. Numerous nation-states have sought to research, develop, produce, stockpile, and use biological agents.[6] Additionally, several well-documented cases display how individuals and small groups have sought to weaponize biological agents for motives ranging from personal avarice to apocalyptic ideologies.[7]

Several drivers are at play. Most recently, the COVID-19 pandemic highlighted severe vulnerabilities in biological threat responses. The strategic impact on the United States was surely not lost on actors with adversarial views toward the nation (and similarly with regard to other countries).[8] Even before this pandemic, the geopolitical strains and security dilemmas facing several countries may have been motivating biological weapons activities within several countries, according to unclassified U.S. government assessments.[9] Added to these factors are dramatic technological advances that are mostly driving incredible benefits to humanity, but that also allow for more accurate and less difficult manipulation of the building blocks of life. Technological breakthroughs are both fueled by and combining with more accessible information and equipment.[10]

While biological weapons are a longstanding threat, the authors of this report and many other experts believe that this threat is worsening. Clear increases in naturally-occurring significant outbreaks and serious biological accidents are equally concerning, as are trends that seem destined to make accidental releases of dangerous pathogens more likely. This section of the report provides a brief overview of each, and the interconnections among them.

BIOLOGICAL WEAPONS

People have been deliberately attempting to poison others or spread disease well before the works of Louis Pasteur and Robert Koch led to the foundations of germ theory - the current prevailing theory that microorganisms known as "pathogens" are the source of disease. Well-documented cases include the British army's use of smallpox-infected gifts against Native Americans in 1763, with the intent of causing a smallpox outbreak, as well as a Confederate physician's attempt to spread yellow fever in Northern cities during the American civil war through clothing contaminated by yellow fever victims.[11]

The early-to-mid 1900s saw the emergence of several state-led biological weapons programs, a feat that was enabled by the spread of germ theory and other advances in life sciences knowledge and capabilities. These programs were unsophisticated by modern standards, yet convinced many actors that biological weapons had unique military and

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6 See Gregory D. Koblentz, *Living Weapons: Biological Warfare and International Security* (Ithaca, NY: Cornell University Press), 2010; Gregory D. Koblentz, "Regime Security: A New Theory for Understanding the Proliferation of Chemical and Biological Weapons," *Contemporary Security Policy* Vol. 34, No. 3, 2013: pp. 501 - 525; Mark Wheelis, Lajos Rozsam, and Malcolm Dando, *Deadly Cultures: Biological Weapons Since 1945* (Cambridge, MA: Harvard University Press, 2009); Milton Leitenberg and Raymond A. Zilinskas, *The Soviet Biological Weapons Program: A History* (Cambridge, MA: Harvard University Press, 2012); and Chandre Gould and Peter Folb, *Project Coast: Apartheid's Chemical and Biological Warfare Programme*, United Nations, 2002.

7 See Jonathan B. Tucker, *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons* (Cambridge, MA: MIT Press, 2000); Robert Jay Lifton, *Destroying the World to Save It: Aum Shinrikyo, Apocalyptic Violence, and the New Global Terrorism* (New York, NY: Henry Holt and Company, LLC, 1999); and W. Seth Carus, *Working Paper - Bioterrorism and Biocrimes: The Illicit Use of Biological Agents Since 1900* (Washington, DC: National Defense University Press), 2001.

8 Christine Parthemore and Andrew Weber, "Op-Ed: COVID-19 May Be Teaching the World a Dangerous Lesson," *Los Angeles Times*, November 12, 2021; Andrea Howard, "The Pandemic and America's Response to Future Bioweapons," *War on the Rocks,* May 1, 2020; and Regan F. Lyon, "The COVID-19 Response Has Uncovered and Increased our Vulnerability to Biological Warfare," *Military Medicine* Vol. 186, No. 7 - 8, 2021: pp. 193 - 196.

9 United States Department of State, *Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments*, April, 2021.

10 National Academies of Sciences, Engineering, and Medicine, *Biodefense in the Age of Synthetic Biology*: pp. 1 - 10.

11 W. Seth Carus, *A Short History of Biological Warfare: From Pre-History to the 21st Century* (Washington, DC: NDU Press, 2017): pp. 2 - 11.

A serviceman takes part in military drills of the Russian Central Military District's Nuclear, Biological and Chemical (NBC) protection troops, in the Sverdlovsk region, Russia. Pavel Lisitsyn / Sputnik via AP

strategic advantages, even if developed with the aim of using them only for retaliation. Nations such as Germany, France, Hungary, Italy, Japan, Poland, Canada, the United Kingdom, the United States and the Soviet Union all saw utility in biological weapons for purposes ranging from tactical use (such as sabotage and eroding an opposing country's military force readiness) to strategic use as a deterrence mechanism.[12]

The Cold War era featured significant movement towards arms control measures to curtail threats by the world's worst weapons. This included the diplomacy that led to the outlawing of such weapons through the Biological Weapons Convention, which entered into force in 1975. As important as this step was, it did not end biological weapons activities, which in this time period began to include new possibilities from the then-recent innovation of genome editing. The largest state bioweapons program during this time was that of the Soviet Union, though this was not known at the time. Between 1972 and 1991 the Soviet Union expanded its existing biological weapons program and amassed the largest biological weapons stockpile in history.[13] The Soviet program included up to 65,000 employees across military and civilian components in dozens of facilities.[14] Its scientists had worked on numerous agents for biological weapons and mass production, and dissemination methods for many of them, and later focused

12 Ibid., pp. 12 - 27.

13 Raymond A. Zilinskas, *The Soviet Biological Weapons Program and its Legacy in Today's Russia* (Washington, DC: NDU Press, 2016).

14 Milton Leitenberg and Raymond A. Zilinskas, *The Soviet Biological Weapons Program: A History* (Cambridge, MA: Harvard University Press, 2012), p. 700.

on engineering pathogens. Just one facility in Stepnogorsk, Kazakhstan, was capable of producing around 300 metric tons of anthrax agent in about 10 months if mobilized in wartime---enough to decimate humanity.[15]

When the Soviet Union disbanded in 1991, significant assets for its biological weapons program were located in the newly-independent states, primarily Kazakhstan. As the scale of the Soviet program became known, the weapons, equipment, facilities, raw materials, and people involved in this program became a top proliferation concern. The United States stepped in and worked hand-in-hand with Kazakhstan and other Soviet successor states to keep countries such as Iran from inheriting Soviet biological weapons capabilities. The lead vehicle for this cooperation was the Cooperative Threat Reduction (CTR) program developed and co-sponsored by Senators Sam Nunn and Richard Lugar, a highly-effective and well-regarded program that continues to provide partner countries with funding and expertise to address biological threats.

Though most countries were signing onto the Biological Weapons Convention (BWC) and complying with its terms, the Soviet Union was not alone in having a biological weapons program. Iraq was extremely concerning in this regard, including the risk of Saddam Hussein using such weapons, just as it had used its chemical weapons arsenal against Iranians and Kurds in the 1980s and targeted use of them within Iraq into the early 1990s. After Iraq's invasion of Kuwait and the first Gulf War, United Nations (U.N.) resolutions required Iraq to comply with the Geneva Protocol and BWC and a U.N. Special Commission (UNSCOM) was established to investigate Iraq's weapons of mass destruction activities and pursue the end of these programs. Through Iraqi-provided information and UNSCOM's work, the international community learned that the country had indeed run an offensive biological weapons program that included anthrax, botulinum toxin, tularemia, wheat rust, and other agents, as well as some work on delivery systems.[16] According to a U.S. government report, if Iraq had used the biological warfare agents that were available to it against U.S. forces, enormous fatalities may have resulted and the Army's medical treatment system would likely have been overtaxed.[17]

As the United States and the international community focused significant efforts on seeing a full end to these biological weapons threats and addressing concerns regarding other countries, the 1990s also brought rising concerns that some terrorist groups could seek to obtain or develop weapons of mass destruction. This was driven home in 1995 when a Japanese cult, Aum Shinrikyo, carried out a sarin gas attack in Tokyo's subway system that killed 12 and injured more than 1,000 people. Later investigations revealed that the group also tried to develop biological weapons, and even sprayed anthrax from an urban rooftop in one test.[18]

The events surrounding September 11, 2001, also left an indelible mark on the United States and its future trajectory. On the heels of the 9/11 terrorist attacks, America experienced biological terrorism on an unprecedented scale through the 2001 anthrax attacks (called the Amerithrax case) which involved the perpetrator mailing letters that contained anthrax spores to prominent senators and several media outlets. As the spores became aerosolized through the mailing process, mailing facilities and recipients were exposed and contaminated, resulting in 5 deaths, another 17 infected, and costing nearly $1 billion in decontamination efforts.[19]

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15 See Zilinskas, The Soviet Biological Weapons Program, pp. 15 - 46; Kenneth Alibek and Jonathan Tucker, "Biological Weapons in the Former Soviet Union: An Interview with Dr. Kenneth Alibek," *Non-Proliferation Review,* Spring-Summer, 1999: pp. 2 - 6; and Michelle Stem Cook and Amy F. Woolf, *CRS Report for Congress*: *Preventing Proliferation of Biological Weapons: U.S. Assistance to the Former Soviet States* (Washington DC: Library of Congress Publishing, 2002): p. 4.

16 Jeanne Guillemin, *Biological Weapons: From the Invention of State-Sponsored Programs to Contemporary Bioterrorism*, (New York: Columbia University Press, 2005): pp. 152-155.

17 U.S. Government Accountability Office, *Chemical and Biological Defense: U.S. Forces Are Not Adequately Equipped to Detect All Threats*, GAO-148623 (Washington, DC: 1993).

18 Please see Hiroshi Takahashi, Paul Keim, Arnold F. Kaufmann, Christine Keys, Kimothy L. Smith, Kiyosu Taniguchi, Sakae Inouye, and Takeshi Kurata, "Bacillus anthracis Bioterrorism Incident, Kameido, Tokyo, 1993," *Emerging Infectious Diseases* Vol. 10. No. 1, 2004: pp. 117 - 120 and Richard Danzig, Marc Sageman, Terrance Leighton, Lloyd Hough, Hidemi Yuki, Rui Kotani, and Zachary M. Hosford, *Aum Shinrikyo: Insights Into How Terrorists Develop Biological and Chemical Weapons, Center for a New American Security*, December 2012.

19 Jeanne Guillemin, *American Anthrax: Fear, Crime, and the Investigation of the Nation's Deadliest Bioterror Attack*, (New York: Times Books, 2011).

As such, concerns regarding biological weapons threats shaped U.S. responses to the 9/11 attacks. This included robust activities aimed at reducing vulnerabilities within the United States and for military personnel operating abroad. These efforts continue today, and often focus on regions of high concern regarding biological weapons activities, such as the Korean Peninsula.

Biological weapons threats also shaped warfare in the following years. In Iraq, the Saddam Hussein regime continued its recalcitrance and lack of transparency. This blended with other factors to drive U.S. and U.K. leaders to allege that Iraq was continuing its WMD activities, with a strong emphasis on biological weapons, in the run-up to the 2003 toppling of the regime. Later, it became clear that the prior UNSCOM work and other efforts contributed to Iraq no longer having biological weapons. These events left significant scars and continue to lead some experts to downplay biological weapons threats out of concern that elevating them may contribute to conflict again in the future.

The international security environment is no less complex today. The COVID-19 pandemic struck at a time when geopolitical, sociocultural, economic, and environmental factors were already drastically changing the security landscape. Nations such as Russia, China, Iran, and North Korea are suspected of possessing biological weapons capabilities and have shown a willingness and ability to engage in gray-zone warfare (i.e. competitive activities between states that are characterized by "intense political, economic, informational, and military competition" that is short of conventional war).[20] The perceived erosion of the norm against the use of chemical weapons has also raised concerns at the highest levels. Many fear this may be a harbinger for the decay of norms against the use of other lethal agents, including biological weapons.

Biological threats are once again becoming intertwined with rising great power competitions. They are also becoming a core element of gray-zone warfare itself in the form of active disinformation and misinformation campaigns. Actors in Iran, China, and Russia have accused the United States of driving COVID-19 as part of what they incorrectly allege are biological weapons activities, just as some actors in the United States share the reverse concern regarding China. In the future, targeted uses of biological weapons may be part of gray-zone operations. For now, the pandemic highlighted again how even just via informational and deception campaigns, mass casualty events can create confusion, extend and drive greater casualties, and even undermine the foundations of democracy in the United States and in other countries across the globe.[21]

These trends are converging with other modern-day factors that are further disrupting the proliferation landscape regarding biological weapons threats. Greater distribution of equipment, materials, and knowledge are lowering certain barriers to entry to these types of weapons. Advances in the ease-of-use and specificity of biotechnology are potentially opening new avenues for biological weapons use.[22] Finally, the emergence of the bioeconomy could exacerbate the already-difficult task of discerning facilities engaged in legitimate work from those engaged in illicit research and development.[23]

It is also important to note that the COVID-19 crisis itself may increase the attractiveness of biological weapons. First, the pandemic has exposed how large-scale biological events can have exceptionally deleterious effects on the

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20 Joseph L. Votel, Charles T. Cleveland, Charles T. Connett, and Will Irwin, "Unconventional Warfare in the Gray Zone," *Joint Forces Quarterly*, 80, 1st Quarter 2016.

21 See Miles Parks, "Few Facts, Millions of Clicks: Fearmongering Vaccine Stories go Viral Online," *NPR*, March 25, 2021; Amir Baherpour and Ali Nouri, "COVID Misinformation is Killing People," *Scientific American*, October 11, 2020; Hallie Miller, "U.S. COVID Vaccination Rate Still Lags Because of Disinformation Campaign, Hopkins Epidemiologist Warns," *Baltimore Sun*, July 21, 2021; and Luiza Bandeira, Nika Aleksejeva, Tessa Knight, and Jean Le Roux, *Weaponzied: How Rumors About COVID-19's Origins Led to a Narrative Arms Race*, The Atlantic Council, 2021.

22 Michael Moodie, "Chapter 14. Options and New Dynamics: Chemical and Biological Weapons Proliferation in 2020," in James W. Wirth and Peter R. Lavoy, *Over the Horizon Proliferation Threats* (Redwood City: Stanford University Press, 2020): pp. 266 - 290.

23 National Academies of Sciences, Engineering, and Medicine, *Safeguarding the Bioeconomy*, (Washington, DC: The National Academies Press, 2020).

international arena. In addition, despite significant work in the decades following the Amerithrax incident, the pandemic has exposed vulnerabilities to U.S. detection of, response to, and recovery from biological events. The potential damage and the perceived weakness of countries like the United States in biodefense capabilities may perversely incentivize some state and non-state actors to explore and pursue offensive biological weapons capabilities.

Therefore, it is in the strategic interest of the United States to be the most attractive partner for countries seeking cooperation and support in enhancing their capacities to mitigate biological threats. Further, there is a clear history and potential incentive for nation-states and sub-state actors to pursue biological weapons for a variety of motivations and outcomes, which means that it behooves the United States, as well as allied and partner countries to work cooperatively and increase the prioritization of efforts to address deliberate biological threats.

NATURALLY-ARISING BIOLOGICAL THREATS

In early January 2020, scientists managed to sequence what was later labeled SARS-CoV-2, a novel coronavirus that had begun circulating in human populations in prior months. While the identification and characterization of the causative virus of COVID-19 was accomplished in an unprecedentedly swift fashion, this effort was unable to prevent its spread around the globe. By March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic, with the United States declaring the pandemic a national emergency shortly afterwards.[24] As of this writing, nearly two years later, the virus is continuing to rampage across the world and evolve.

Unfortunately, experts project that severe outbreaks with the potential to reach pandemic scale will occur more frequently without significant and effective interventions. Outbreaks of pandemic-potential infectious diseases like Middle-Eastern Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) reveal that infectious disease emergence is increasing in frequency.[25] Further, climate change, coupled with greater human-animal interactions due to deforestation and economic development, is contributing to increased disease outbreaks around the world. Many are coronaviruses and other respiratory illnesses that commonly spill over into human populations from animals like bats and birds.[26]

To be clear: naturally-arising disease threats can reach catastrophic scales, and they are a strategic threat in and of themselves if they are not addressed effectively. At the time of writing, COVID-19 has killed hundreds of thousands of Americans (and rising), infected the nation's then-president, sent the Joint Chiefs of Staff into quarantine, affected the operations of naval vessels and military bases, complicated operations to pull back the U.S. presence in Afghanistan, strained relations with both allies and countries with adversarial views toward the United States, and countless other effects.

Therefore, it is strategic for the United States to consider the various ways that biological threats from natural origins can affect the nation at a significant scale. Natural biological threats are likely to emerge in an accelerated fashion via spillover effects due to anthropogenic forces driving climate change and ecological disruption---actions that are precipitating greater interactions between animal and human populations.

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24 World Health Organization, "WHO Director-General's Opening Remarks at the Media Briefing on COVID-19 - 11 March 2020," March 11, 2020; and U.S. White House, "Notice on the Continuation of the National Emergency Concerning Coronavirus Disease 2019 (COVID-19) Pandemic," February 24, 2021.

25 Hamish de Bretton-Gordon, "Covid-19 Has Revealed Just How Vulnerable We Are to Biosecurity Threats," *CNN*, December 20, 2020.

26 Abraham Lustgarten, "How Climate Change is Contributing to Skyrocketing Rates of Infectious Disease," *ProPublica*, May 7, 2020.

USAID PREDICT completes sampling visit to Ratchaburi Province. Richard Nyberg/USAID

The increased likelihood of both novel and re-emerging infectious diseases from natural sources is an enduring threat to public health broadly. The changing microbial landscape will also affect future military readiness and logistics for monitoring, maintaining, and treating service members on overseas missions. Defense forces must be prepared to operate in diverse environments. Modern phenomena like climate change add a twist: the changing pathogen terroir of an operational region requires careful consideration of the protection and medicines that service members may require in the line of duty. These dynamics also significantly change how operations are run for detecting, mitigating, and treating affected members in a field setting.[27]

Additionally, the natural spread and changing landscape of microbes has potential implications for deliberate biological threats. As pathogens migrate to new areas, states may be able to acquire new pathogen options for biological weapons research, development, production, and use. Past biological weapons programs have had components that acquired pathogens from the natural environment. The most prominent and well-known of these efforts was how the Soviet Union used a branch of the public health system known as the Anti-Plague System. While ostensibly used for health security and biodefense purposes, this system also supplied strains of virulent pathogens to civilian and military biological facilities, likely including the causative agents for anthrax, tularemia, and plague.[28]

Importantly, naturally-occurring disease threats also influence how accidents may arise. One pathway is from activities such as gain-of-function research and efforts to uncover new viruses from nature, and how these pathogens may evolve to affect animal and human populations, which are seen as potential methods of enhancing public health goals. However, such work can also elucidate knowledge that can be deliberately misused, or that can increase the risk of accidents. For example, if enhanced viruses are not handled in ways that minimize their risk of accidental release before their full human effects are known, the results can be catastrophic.

27 Matthew Cox, "The Next Major Battlefield Threat Facing U.S. Troops May Be Undetectable," *Military.com*, September 2, 2020.

28 Raymond A. Zilinskas, "The Anti-Plague System and the Soviet Biological Warfare Program," *Critical Reviews in Microbiology,* No. 32, 2006: pp. 47 - 64.

Natural disease threats are also fueling a drive to create more "high-containment labs" to ostensibly conduct research deemed necessary for mitigating future outbreaks. In some cases this measure may be warranted, but it can also increase the risk of biological events due to human error and other accidental sources.[29] These labs can also be used to house research that crosses the line into offensive biological weapons work.

BIOLOGICAL ACCIDENTS

There are several historical examples of lab accidents threatening public health in the United States. For instance, in 2014 the CDC mistakenly shipped a sample of the highly pathogenic H5N1 influenza to a BSL-2 lab, where it was used in experiments until researchers realized the error.[30] In 2015, a Utah Army lab distributed live anthrax to 194 other labs, putting workers at risk.[31] While there were no confirmed exposures in either of these incidents, both were close calls that highlight the necessity of maintaining tight biosafety standards. Human error can have drastic consequences, even when there is no ill intent.

A well-known example of a breach in biosafety outside of the United States occurred on April 2, 1979 in Sverdlovsk (now Ekaterinburg) with the accidental release of anthrax spores from a Soviet bioweapons facility. This release caused a local outbreak that resulted in at least one hundred deaths.[32] Accidents like this one may be covered up if they stem from violations of the BWC's international ban on bioweapons. This, combined with the specter a lab accident can bring to a dual-use research institution, means the number of lab accidents is likely under-reported and the effects of accidental releases underestimated.

Advances in genetic engineering and synthetic biology have made it easier than ever to modify pathogens to be more dangerous, heightening the risks of biological accidents. Similarly, experiments involving serial infection of animals have demonstrated the potential to increase the transmissibility of viruses. For instance, a controversial 2012 study used a combination of genetic engineering and serial infection of ferrets to direct the evolution of the avian H5N1 flu into a variant capable of airborne transmission in mammals.[33] Additionally, as researchers try to detect and prepare for the next pandemic by seeking out viruses in nature to study, the risk of inadvertently contracting and introducing a virus to the community may rise if strong protocols are not adhered to.[34] While biodefense and natural pandemic research are crucial, a responsible approach is necessary.

The number of high-containment research labs throughout the world is rapidly growing.[35] Though this expansion is largely happening in the name of biodefense and public health, the lack of a standardized approach to biosafety has hampered trust in such institutions. In many countries, governments do not have a clear, centralized understanding of what research involving dangerous pathogens is being conducted within their own borders.

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29 See Jeff Tollefson, "Why Deforestation and Extinctions Make Pandemics More Likely," *Nature*, August 7, 2020 and Joseph Rodgers, Filippa Lentzos, Gregory D. Koblentz, and Minh Ly, "How To Make Sure the Labs Researching the Most Dangerous Pathogens are Safe and Secure," *Bulletin of the Atomic Scientists*, July 2, 2021.

30 Diana Fine, "CDC Botched Handling of Deadly Flu Virus," *Scientific American*, July 11, 2014.

31 Dan Lamoth, "Pentagon: Live anthrax inadvertently distributed by Army laboratory," *Washington Post*, May 27, 2015.

32 Ken Alibek, *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World*, (New York, New York: Random House Publishing, Inc., 1999).

33 Ron A. M. Foucier et al., "Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets," *Science* Vol. 336, No. 6088, 2021: pp. 1534 -1541.

34 Jeffrey Marlow, "The Virus Hunters," *Scientific American*, May 26, 2017.

35 Hamish de Bretton-Gordon, "Biosecurity in the Wake of COVID-19: The Urgent Action Needed," United States Military Academy West Point, Combatting Terrorism Center, December 2020.

THE SPECTRUM OF BIOLOGICAL THREATS

The policy roadmap at the heart of this handbook, drawing from the expertise of the authors and many experts with whom CSR has collaborated, focuses on the overlap among deliberate, accidental, and natural biological threats. Many of the technologies and policy responses, and much of the expertise required for progress in all of these areas are common.

The U.S. approach must also recognize when steps needed to address deliberate, accidental, and naturally-arising biological threats pose unique requirements. For example, the U.S. Centers for Disease Control and Prevention's (CDC's) mission is far broader than the catastrophic biological threats at the center of this report, and those functions must be supported. Likewise, the U.S. Department of Defense has some unique needs and capacities related to deliberate biological weapons threats that it must safeguard and which are not provided by other agencies.

This report offers a number of examples of the unique roles, responsibilities, authorities, and capacities of many key U.S. entities. It also aims to tell the larger story of how these programs intertwine and can be built into a much more effective system. Moreover, keeping a broad view is necessary given the evolving character of biological threats, and the concern that actors may consider developing and deploying biological weapons under the cover that they may appear to be natural outbreaks or accidental releases.

The past few decades of advancements against Ebola provide one example. The U.S. government viewed Ebola as a potential biological weapon threat---and it is an endemic disease in places where U.S. defense personnel, including Special Forces, may operate.

The largest Ebola outbreak in history began in Guinea, West Africa, in 2013. This outbreak ultimately resulted in more than 11,000 deaths in Guinea, Liberia, and Sierra Leone by the time the WHO lifted the Public Health Emergency of International Concern status in the region in 2016.[36] In January 2021, in the midst of the COVID-19 pandemic, an Ebola outbreak was declared in Guinea again. According to Dr. Ibrahima Socé Fall, the Assistant Director-General of the WHO, a "ring method" around confirmed cases of Ebola in Guinea was being applied to stop the spread: within a certain geographic space, all those with possible exposure to Ebola were vaccinated.[37]

Ebola was long neglected by the private sector, and given its force health and weaponization concerns, the U.S. Department of Defense was one of the only entities that filled that gap by funding early-stage research and development on vaccines, treatments, and diagnostic tools that fit the often-remote and low-resource environments in which they were likely to be needed. The Chemical and Biological Defense Program (CBDP), explored in greater depth later in this report, was pivotal in vaccine development. When it became clear that the 2014 outbreak was getting out of hand, work that had already been done by CBDP and other agencies positioned a vaccine candidate to be accelerated with the hope of being authorized for use to save lives. This later came to fruition, including by various government agencies continuing to advance these vaccines and other tools when national concern regarding Ebola dropped.

Without past biodefense investments, the world would likely not have good Ebola vaccines, therapeutics, and the advanced diagnostic tools that are in use today.

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36 U.S. Centers for Disease Control and Prevention, "2014 - 2016 Ebola Outbreak in West Africa," March 8, 2019.

37 United Nations,"1,600 Vaccinated in Guinea Ebola Virus Outbreak but More Jabs Needed: WHO," March 5, 2021.

Furthermore, the United States needs diverse faces in its international partnership efforts to address the full range of biological threats. Given the sensitive nature of biological threats and solutions, at times progress with a specific country or laboratory is most likely to occur via universities, nongovernmental organizations, or the U.S. CDC. In other cases, having a defense agency presence at the forefront is best. As shown in this report, U.S. agencies have been skillful and thoughtful in considering the best frontline actors for different lines of effort in addressing biological threats.

Getting this right will help shape risks and risk reduction across this century, in which positive---and at times destructive---uses of biotechnology will be a defining feature. This task begins with setting a bold vision for how the United States will approach its work to address catastrophic biological threats.

IV. A NEW VISION FOR ADDRESSING THE THREATS

SETTING A BOLD VISION

Creating a new future where the United States aggressively addresses catastrophic biological risks and maintains this work as a high priority will require several key elements. One of the most important is a bold, moonshot-level vision that inspires people and creates political momentum for increasing resources. Such a vision must be clear and compelling, and it must be big enough to drive transformative changes---not the incremental improvements the U.S. government has often pursued in the past.

In terms of naturally-arising biological risks, the United States is already beginning to embrace an ideal vision: *preventing future pandemics*. With the expansion of robust early warning capacities, rapid responses, and improved international coordination, the nation's aim should be to stop outbreaks from growing to pandemic scale---not simply enduring them and accepting the lives lost and damage to health security, national security and the economy that pandemics can cause.

This report recommends continued, strong progress toward the vision of preventing future pandemics. It also recommends a complementary, robust U.S. strategy regarding deliberate biological threats---one which will require far more significant shifts in the nation's goals and policies. It therefore proposes that U.S. leaders set the following vision for the nation:

> *The United States should lead the world in making biological weapons the first category of weapons of mass destruction to be effectively eliminated or rendered obsolete.*

To advance this aspect of a strong U.S. vision, the report recommends that national security leaders adopt a **"deterrence by denial"** strategy that focuses on ultimately denying an attacker success in their likely aims regarding biological weapons, such as causing mass casualties, mass confusion, and erosion of operational capabilities. This would both mark several major policy changes for the United States and significantly improve how U.S. federal agencies leverage the innovation occurring across the nation. As this shift in the nation's approach would require more changes from its current path than is the case for pandemic prevention, it is the focus of much of this handbook.

This vision aligns with the current momentum of the United States (and many other countries around the world) to prevent the next pandemics that could emerge from naturally-occuring diseases or accidental releases. It extends similar principles and complementary programmatic investments to address deliberate biological threats as well.

As a show of commitment to this comprehensive vision, the President should articulate these views and goals through a "Prague speech" equivalent on preventing future pandemics and eliminating biological weapons as a mass destruction threat---potentially surrounding the Biological Weapons Convention (BWC) Review Conference in 2022.

CSR has explored this concept extensively for several years in collaboration with government experts, academic leaders, and private sector innovators, including via a series of discussions held in collaboration with Sandia National Laboratories. These discussions have highlighted widespread agreement across U.S. stakeholders that the technologies now exist to achieve this vision. In other words, it is a matter of when and how, not if.

UPDATING U.S. STRATEGY

Preventing pandemics and ending the mass-destruction threat of biological weapons is no simple task. Infectious diseases and pathogens that may be weaponized will always be present, as will adversarial relations across international actors.

Yet the visibly-devastating effects of COVID-19 on the United States and the world, the evolving threats and solutions in this space, and other dynamics all point toward this being the optimal time for implementing this strategic shift for the United States.

The current National Biodefense Strategy, while strong, needs this upgrade. The current U.S. approach of "biological risk management" is simply not aggressive nor inspiring enough. The COVID-19 crisis has shown the extreme damage biological risks pose to the United States and the world. The nation's approach must center on preventing pandemics and other extreme biological risks, not just managing them.

In the case of biological weapons, the current U.S. defense strategy is suboptimal in three main areas. First, current U.S. policy holds that deterring biological weapons is conducted by the threat of punishment with nuclear weapons.[38] In this case, such deterrence by threat is not likely to be seen as credible by those the United States wishes to deter. Second, U.S. biodefense is driven by ensuring that military forces can operate in an environment in which biological weapons are used; this may be a component of deterrence but in itself is not an optimal end state, and points to the nation over-relying on the threat of nuclear retaliation being effective (including in cases where an adversary may pursue smaller-scale use of biological weapons or attacks that are highly difficult to distinguish from a natural outbreak).

"Deterrence by denial" in the bioweapons context is a more appropriate strategy for the United States than the status quo, in particular if it is jointly pursued by allies and other nations in the future. Just as this theory has been applied with regard to conventional armed forces and postures, the aim is to deter an adversary from carrying out an attack in the first place, knowing that consequences (even if it is with conventional, not nuclear, arms) could be severe even if the attack is likely to be ineffective. As RAND expert Michael Mazarr described in 2018, "most classic studies suggest that denial strategies are inherently more reliable than punishment strategies. Steps taken to deny, such as placing significant military capabilities directly in the path of an aggressor, speak loudly and clearly."[39]

The deterrence by denial approach has been in the background of U.S. national biodefense strategies and national security strategies for some time. However, it has not explicitly been the central driver of U.S. strategy in large part

38 Lulu Garcia-Navarros, "The Other NPR: Nuclear Posture Review," *National Public Radio*, January 28, 2018.

39 Michael J. Mazarr, "Understanding Deterrence," *RAND Corporation*, 2018.

because the technologies and practices needed to make it a reality were envisioned - and in many cases in development - but not yet mature enough to be deployed broadly.

As a result of decades of basic scientific achievements and investments, this has changed. The world has seen incredible breakthroughs across individual and converging technologies such as biotechnology, medicine, robotics, AI and machine learning, and other components of advanced manufacturing. Technological readiness is no longer a limiting factor in implementing the vision this report recommends. As shown in examples throughout this report, the U.S. Departments of Defense and Health and Human Services have been core drivers of these advances, alongside world class academic labs and innovative companies.

Put together, these advances can create a layered, systemic approach to rapidly halting emerging biological threats that would otherwise potentially create mass effects. Components of such a system include:

- Developing, testing, and deploying existing and emerging technologies to better detect pathogens of concern in a variety of contexts.

- Enhancing and accelerating rapid medical countermeasure capabilities such that the timeline from pathogen identification to countermeasure testing and deployment is drastically reduced in a variety of settings. A 2021 White House plan set goals that are appropriate but need to be further accelerated over time: to develop, test, and review "a safe and effective vaccine against any human virus within 100 days after the recognition of a potential emerging pandemic threat," and "enable production of enough vaccine for the entire United States population within 130 days and for the global population within 200 days."[40]

- Encouraging greater engagement from the private sector to provide promising and innovative new tools and technologies, and greater fluidity in collaboration.

- Exploring new methods and technologies to enhance U.S. and international understanding of biological threats as they evolve, and verify peaceful uses of biotechnologies.

The United States is already advancing significantly in these areas. Some progress has been slow and steady, and in other areas the urgency of COVID-19 responses have brought new tools into use faster than ever before. As the first real road test of many of these capabilities, the COVID-19 pandemic responses have been rough, and more work is needed. Yet because this progress is already underway, now is the best possible time to continue aggressive movement in this direction.

In the coming years, there are several prime opportunities to continue pivoting U.S. strategy and plans in this manner. The visions of pandemic prevention and robbing biological weapons of their mass-destruction potential need to be firmly embedded in forthcoming strategy updates by the United States: the next National Security Strategy, National Defense Strategy, and National Biodefense Strategy, in addition to supporting policy documents drafted by the relevant departments and agencies. These instructions will then need to be translated into budgets and programs, for which Executive Orders and instruction from the Office of Management and Budget will be important.

40 U.S. White House, "American Pandemic Preparedness: Transforming Our Capabilities," September 2021: p. 11.

IMPLEMENTING THE STRATEGY

The next sections of this report focus on ideas for implementing this bold vision. Each chapter details specific programs and activities carried out by many of the U.S. government offices most essential to implementation. The issues and ideas presented in each chapter stem from individual interviews and private roundtable discussions CSR held with current and former leaders and staff of these organizations, as well as the personal experiences and expertise of the authors. It also explores several sets of critical activities, such as rapid development and manufacturing of medical countermeasures, to highlight their cross-agency nature. Throughout the report, we include text boxes on tips that U.S. officials may wish to use for implementing this strategy.

Finally, any new strategy will fail without resources. This report therefore proposes an investment strategy by the United States government that we call "10+10 over 10."

This concept would equate to $10 billion per year for ten years for health security and direct pandemic prevention capacity building, plus $10 billion per year for ten years for countering biological weapons threats, biological defenses, and biological threat reduction partnership programs. As the COVID-19 pandemic will cost the nation more than $16 trillion for just one dangerous pathogen, this represents a relatively modest but high-impact investment for U.S. national security and for the national bio-industrial base.[41]

Noting that these investments should be pursued in complementary ways but often overlap in function and gains made, in *Part VII* of this handbook we provide a schematic proposal for how such investments may be distributed across U.S. government agencies. Additionally, substantial private sector and civil society contributions to addressing catastrophic biological risks in the coming years will increase the odds of this strategy's success.

41 David M. Cutler and Lawrence H. Summers, "The COVID-19 Pandemic and the $16 Trillion Virus," *JAMA* 324, no. 15 (2020): pp. 1495-1496.

V. RECOMMENDATIONS BY U.S. GOVERNMENT DEPARTMENT & AGENCY

INTRODUCTION

In the United States, responsibility for addressing biological threats is shared across multiple departments and agencies, and numerous offices and programs within each. This is natural given the legal authorities that Congress has conferred on different agencies and the need to address biological threats spanning multiple agencies' missions. After all, countering biological threats is an imperative for national security, public health, economic competitiveness, agricultural productivity, and beyond.

This report's primary focus is on *catastrophic biological threats*---high-consequence infectious disease threats that could grow to a scale of systemic disruption to international security if not stopped quickly. For this reason, it does not provide comprehensive details regarding broader public health functions, such as CDC programs that focus on chronic, non-infectious diseases. Such work is critical and should be supported robustly, but is outside of the scope of this work.

In this context, the following section provides information on many of the key agencies and programs that will be critical to creating systemic progress. That is, the kind of progress needed for the United States to embrace a dual strategy of *deterrence by denial* for biological weapons threats and *preventing future pandemics* from natural or accidental sources.

The Pentagon. Sgt. 1st Class Marisol Walker/Office of the Chief, Army Reserve

THE U.S. DEPARTMENT OF DEFENSE

The U.S. Department of Defense has contributed to historical achievements in addressing biological threats. In many cases, U.S. defense personnel have driven and led such work. This includes work on disease threats often ignored by private companies and other government agencies, but that were of special concern for defense forces deployed globally who may have been at a heightened risk of being the target of deliberate biological attacks. The following are examples of some key accomplishments.

- The Department's Cooperative Threat Reduction Program collaborated with other nations to secure and then eliminate industrial-scale former Soviet biological weapons infrastructure that was once able to produce enough anthrax and other biological weapons to kill everyone on Earth.

- The Chemical and Biological Defense Program conducted long-term efforts to find solutions for Ebola, given concerns that it may be weaponized and that U.S. forces may need to operate in regions where it is endemic and be exposed, leading to the first-ever vaccine as well as new diagnostic tools and therapeutics.

- In its efforts to develop rapid responses for potential future engineered biological weapons, the Defense Advanced Research Projects Agency (DARPA) played a key role in advancing the mRNA vaccine platform

technologies that became a core part of developing COVID-19 vaccines in record time.[42] Other Defense offices later contributed to advancing these vaccines through Operation Warp Speed.

Despite such accomplishments, the Department's significant contributions are often overlooked and insufficiently prioritized. It is urgent that policymakers reverse this. The following sections detail just why this work is so important, and recommendations for how it should be shaped in the years ahead, for several defense programs: the Chemical and Biological Defense Program, the Biological Threat Reduction Program, DARPA, and the United States Army Medical Research Institute of Infectious Diseases (USAMRIID). Across these programs, many are carried out by the Defense Threat Reduction Agency (DTRA) and the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND). More broadly, the Department's leaders for research and engineering, acquisition, treaty compliance, and the Department of the Army are all key players as well.

42 U.S. Department of Defense, Defense Advanced Research Projects Agency, *Adept: Protect*, 2020.

LEADERSHIP AND INSTRUCTION MECHANISMS FOR ADVANCING DEPARTMENT OF DEFENSE EFFORTS

Pursuing the policy shifts, ideas, and programmatic developments recommended in this report will require both good leaders with a clear vision and their skillful use of existing bureaucratic processes and mechanisms for ensuring the Department of Defense (DoD) pivots in the necessary directions. This text box presents several ideas along these lines, some of which must come from within DoD and some of which must be conducted externally.

Reward Progress. Military and civilian personnel who are excelling in creatively advancing U.S. efforts to address catastrophic biological risks should be rewarded for such efforts. There are numerous awards that DoD regularly gives for specific achievements and strong, steady-state collaboration in reducing threats to the nation. DoD leaders who have bio as part of their portfolios should work with their teams to identify and reward progress toward "deterrence by denial" and making biological weapons obsolete as a mass destruction threat---and use these occasions to communicate to their workforces the importance of progress in this direction.

Conduct Regular Posture Reviews. DoD should conduct reviews of its strategy, plans, programs, and resources for addressing biological weapons and other biological threats to national security, similar to such periodic reviews regarding the U.S. nuclear posture and threats, and countries of high concern. This should serve as a mechanism to identify what should be changed, accelerated, eliminated, or expanded. It should also include a health check on how DoD testing and evaluation capabilities are being leveraged and coordinated with the private sector to create a strong bio-industrial base and supply chain readiness. Finally, such a review should also identify new ideas for how defense requirements and partnership arrangements can be best leveraged and refined to maximize DoD's acquisition demand pull.

Enshrine Updates in Action Memos and Follow Up. New strategic and programmatic guidance, such as what may stem from regular posture reviews, should consistently be captured in action memos to the correct offices. These ensure that leadership directions are clear, establish accountability, and provide other stakeholders with top-cover in case there is reluctance to make necessary changes. Such memos should specifically instruct where planning and budgeting changes may be warranted, and senior leaders should set processes for following up to ensure guidance is implemented (ideally on a regular basis, not just toward the end of planning and budgeting cycles).

Convey Budget Guidance. The allocation of resources will matter significantly for the nation's ability to address catastrophic biological risks in the coming years. The Office of Management and Budget should send clear guidance to DoD leaders regarding strategic direction from the White House to prioritize resources for addressing biological threats and include specific focus areas (for example, in expanding international partnerships for biological threat reduction, expanding early warning capabilities, etc.).

Keep the Executive Office of the President Leadership Updated. The leaders and staff for countering biological threats at the National Security Council and Office of Science and Technology Policy, respectively, should set up intelligence updates and interagency program briefings on biological weapons risks for key leaders on a regular basis. They should bring in key leaders from DoD, the intelligence community, and the Department of State if helpful in conveying the prioritization of this issue and developing coordinated, ambitious responses.

Declassify Biological Threat Information When Possible. The National Security Council is ideally positioned to set a review process to determine if and when any estimates or details of biological weapons concerns can be declassified and shared with the public (e.g., by the Director of National Intelligence's Annual Threat Assessment testimony to Congress). More transparency regarding the threats may help improve public and Congressional understanding of the urgency of the threat and help build momentum for more ambitious national policies and investments. This, in turn, could help balance against potential pressures to resort to kinetic military action regarding such threats, and create political urgency for diplomatic and technological solutions.

U.S. Navy Cmdr. Brianna Rupp, a preventative medicine physician from the Navy and Marine Corps Public Health Center, takes a survey from a U.S. Sailor, assigned to the aircraft carrier USS Theodore Roosevelt (CVN 71), as part of a public health outbreak investigation April 22, 2020. Mass Communication Specialist 1st Class Chris Liaghat/U.S. Navy photo.

THE CHEMICAL AND BIOLOGICAL DEFENSE PROGRAM[43]

The Department of Defense's Chemical and Biological Defense Program (CBDP) is the center of gravity for biodefense and the department's largest source of funding for research on the subject. CBDP was the home of one of the first initiatives to drastically speed up development of medical countermeasures against new biological threats. The program was called the Transformational Medical Technologies Initiative, and early successes include the creation of a therapeutic against the 2009 swine flu.[44] This rapid-response approach, which the CBDP continues to champion, is critical for addressing biological threats before they impact U.S. national security.

The CBDP must continue to play this central role, including via support for versatile technologies that are essential for addressing biological weapons threats and helpful in dealing with lab accidents and fighting emerging infectious diseases. This will take reversing the erosion of the CBDP's budget that has occurred over the last decade, including during the COVID-19 pandemic.

CBDP's activities form a significant national asset. It makes unique advances in our understanding of biological threats, drives development of new tools for addressing them, takes these tools through testing and evaluation to avoid promising investments hitting the proverbial valley of death, and works with allies and partners to deploy and

43 Much of the text in this section is drawn directly from Bill Beaver, Yong-Bee Lim, Christine Parthemore, and Andy Weber, "Key U.S. Initiatives for Addressing Biological Threats Part 1," Council on Strategic Risks, April 9, 2021.

44 David E. Hoffman, "Going Viral," *The New Yorker*, January 23, 2011.

improve new technologies. Yet there is a disturbing downward trend in this program's resources against biological threats, including cuts made during a historic pandemic, and other issues. In this section we detail near-term recommendations for Pentagon leaders, Congressional members, and other stakeholders.

The process of maximizing CBDP's contributions to countering biological threats should begin by roughly doubling CBDP's funding to at least $2 billion in the next year, to be increased to the $6.5 billion-to-$7 billion annual budget range over the following decade. While such investments should be aimed at addressing biological weapons threats, they should be also seen as part of a whole-of-government surge to never again allow the nation to experience the kinds of mass effects the COVID-19 pandemic has wrought. Among others, key investment areas should include nucleic-acid based therapeutics, a new approach that relies on gene encoding like the highest efficacy COVID-19 vaccines, and field- and clinic-deployable early-detection technology that can identify any pathogen by reading its genetic material. To put these investments to best use, the program's leaders should expand international cooperation, launch annual drills to test and evaluate rapid-response capabilities, ensure that intelligence on these threats reaches high-level defense decision-makers, and more. These investments and capabilities are not a special interest for the military alone, but one that may be critical to the entire U.S. public's resilience to biological threats.

BACKGROUND

The CBDP's critical role can be seen in the history of efforts to combat Ebola. The U.S. government views Ebola as a potential biological weapon threat---and it is an endemic disease in places where U.S. defense personnel, including Special Forces, may operate. In late 2013 in Guinea, West Africa, the largest recorded Ebola outbreak in history began, killing 11,000 through 2016.[45] In January 2021, in the midst of the COVID-19 pandemic, an Ebola outbreak was declared in Guinea again.[46] According to Dr. Ibrahima Socé Fall, the Assistant Director-General of the World Health Organization (WHO), a "ring method" around confirmed cases of Ebola in Guinea was being applied to stop the spread: within a certain geographic space, all those with possible exposure to Ebola are vaccinated.[47]

Ebola was long neglected by the private sector, and given its force health and weaponization concerns, DoD was one of the only entities that filled that gap by funding early-stage research and development on vaccines and treatments. The CBDP was pivotal in vaccine development, and this case is illustrative in understanding the various responsibilities the program has. When it was clear that the 2014 outbreak was getting out of hand, work that had already been done by CBDP and other civilian and defense agencies positioned a vaccine candidate to be accelerated with the hope of being authorized for use to save lives. However, once that specific outbreak abated, attention dropped again. CBDP and other DoD programs played key roles in ensuring that work on the vaccine continued, preventing significant past investments from being left by the wayside. Along this journey, CBDP's contributions included accelerated vaccine development, including in research and development and clinical trials; as well as testing and evaluation, creating treatment infrastructure, developing an FDA-approved Ebola virus diagnostic, and deploying therapeutic drugs.[48]

45 World Health Organization Ebola Response Team, "After Ebola in West Africa - Unpredictable Risks, Preventable Epidemics," *The New England Journal of Medicine* 375, 2016: pp. 587 - 596.

46 World Health Organization, "Ebola Virus Disease – Guinea - WHO," June 19, 2021.

47 United Nations, "1,600 Vaccinated."

48 Crystal Boddie, "Federal Funding in Support of Ebola Medical Countermeasures R&D," *Health Security* Vol. 13, No. 1, 2015: pp. 3 - 8.

CBDP'S HISTORY AND WORK, IN BRIEF

The program is an umbrella organization under the Office of the Secretary of Defense and is responsible for various defense-wide chemical and biological defense activities. It was created through Congressional action in November 1993 after the First Gulf War exposed U.S vulnerabilities. Chemical and biological defense activity had previously been the responsibility of the Department of the Army. According to a government report, if Iraq had used the biological warfare agents that were available to it, such as anthrax and botulinum toxin, there could have been enormous fatalities and the Army's medical treatment system would have been overtaxed.[49] At that time, limited anthrax vaccinations were available, and the sole source of an essential ingredient for botulinum antitoxin was an elderly horse named First Flight.[50] The creation of the CBDP was meant to ensure that the biological defense mission received the attention and funding that it deserved.

Traditionally, the program's primary responsibility is viewed as protecting military personnel from deliberate biological threats. While the focus is on weaponized pathogens, this overlaps with natural disease threats in many cases (such as with Ebola). Additionally, one of many challenges of biological weapons is that they may appear to be of natural origin.

Likewise, solutions to biological threats largely overlap no matter their origin. In that regard, the skills and capabilities resident in the CBDP lend themselves to countering all biological threats. Further, as the COVID-19 pandemic shows, all such threats are of significant strategic concern and can threaten defense personnel directly.

As a broad enterprise, the CBDP unites several DoD organizations that conduct research, development, testing, and procurement of technologies against biological threats. The Joint Science and Technology Office at the Defense Threat Reduction Agency is generally responsible for early-stage research and development. For the Ebola vaccine, the agency contracted with a small biotech company to speed up development and aid in early-stage testing. After the vaccine transitioned to later-stage development, another part of the program, the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense, which also is responsible for procurement, helped conduct late-stage clinical trials.[51] Much of this work is conducted in close collaboration with other U.S. government agencies such as the U.S. Department of Health and Human Services, as well as with nongovernmental partners[52].

Such collaborative relationships extend to critical international partnerships. In the Ebola case, CBDP personnel worked closely with the Public Health Agency of Canada and the WHO. These relationships directly bolster U.S. and global defenses against biological threats, as well as chemical and other weapons of mass destruction. For instance, the security and potential use of the Syrian chemical weapons stockpile became a significant concern after civil war ensued in 2011. This issue rose after the Syrian government's use of sarin (a nerve agent) and later chlorine attacks against its own citizens. Early in this time period, the United States was in short supply of delivery mechanisms for treatments that are required quickly to prevent death from sarin.[53] Via its longstanding relationships, the CBDP identified an Israeli company to fill this need and guided them through the process for the U.S. Food and Drug Administration's (FDA's) Emergency Use Authorization to ensure the availability of antidotes and auto-injectors for U.S. military personnel and others.[54]

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49 U.S. Government Accountability Office, *Chemical and Biological Defense.*

50 Carolyn H. Crowley, "Race for a Remedy," *The Smithsonian,* December, 2000.

51 Hannah Feldman and Rachel Overman, U.S. Department of Defense, JPEO-CBRND, "JPEO-CBRND Supports International Partners in Congo Ebola Outbreak," January 16, 2019.

52 Darnell Gardner, U.S. Department of Defense, Military Health System, "DTRA Contributes to Historic Ebola Vaccine Effort," January 17, 2020.

53 Alicia Mundy, "Sarin Antidote Is Hit With Supply Problems in U.S.," *Wall Street Journal,* September 13, 2013.

54 Steven Lusher, U.S. Department of Defense, JPEO-CBRND, "MCS Instrumental in EUA Approval of Nerve Agent Autoinjector," November 13, 2017.

To facilitate this kind of work on urgent needs as well as longer-term solutions, the CBDP maintains a broad network including close allies such as the United Kingdom, Canada, and Australia.[55] It has worked closely with the Republic of Korea (ROK) on biological defense, a concern in the region because of suspected biological weapons activity in North Korea.[56] Biological defense activities were featured in a series of multi-year, ROK-U.S. exercises called Able Response. Based on scenarios of naturally-occurring outbreaks, over the course of several years these exercises helped both countries identify gaps and needs, test new technologies for disease detection and responses, improve cross-agency coordination, and more.[57] With these capability improvements, it is not surprising that the ROK was among the world's leading countries in early detection and response to COVID-19 when it emerged.

These exercises and relationships have incredible value in directly informing research, development, and acquisition plans to help keep DoD ahead of biological threats and investing in the best technologies and tools for countering them. Moreover, international cooperation is especially important as biological threats are global in nature and difficult to fight alone.[58]

To all of this work, CBDP brings significant capacity for handling some of the most dangerous pathogens for testing and evaluation of early detection technologies and countermeasures. The Dugway Proving Ground, one of the main research, development, testing and evaluation facilities supporting the CBDP, is a chemical and biological agent defense testing ground and is focused on methods of detection and neutralization. In 2015, the largest test chamber in the world, the Whole System Live Agent Test Chamber, was completed at Dugway and is now being used to test technologies for detecting weaponized biological agents.[59] The Dugway Proving Ground handles biological agents categorized as BSL-3, which are dangerous but generally have existing treatments.

The U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) at Fort Detrick, Maryland, operates a BSL-4 lab and allows for testing of treatments of diseases for which no known treatments are available. The institute often conducts testing and evaluation using an FDA process for animal testing, which is required when doing so on a human would be unethical or unfeasible. The institute and others like it in the DoD house the facilities and expertise that allow these tests on the most dangerous pathogens to be conducted.

EVOLVING WITH AND DRIVING TECHNOLOGICAL CHANGE

Throughout its history, the CBDP has worked to counter specific, identified biological threats that the government classifies as having the potential to be weaponized. However, within the program, there is an ongoing shift toward a more flexible approach, which should be a key feature of its future.

In 2004, an accident occurred at one of the premier research laboratories of the CBDP. A researcher working at USAMRIID accidentally pricked themselves with a needle being used to inject mice with the Ebola Virus. The researcher was placed in a medical isolation unit at Fort Detrick nicknamed "the slammer" by employees.[60] A

55 Robert Moeller, U.S. Department of Defense, JPEO-CBRND, "Chemical, Biological, and Radiological Defense Memorandum of Understanding," May 2007.

56 Sangwoo Tak, Anton Jareb, Suon Choi, Marvin Sikes, Yeon Hwa Choi, and Heyong-wook Boo, "Enhancing 'Whole-of-Government' Response to Biological Events in Korea: Able Response 2014," *Osong Public Health and Research Perspectives* Vol. 9, No. 1, 2018: pp. 32 - 35.

57 Ibid., and professional experiences of two of this report's authors.

58 U.S. White House, "Interim National Security Strategic Guidance," March 3, 2021.

59 Gian Volpicelli, "Inside the Open-Air Lab Testing Viruses and Deadly Chemicals," *WIRED UK*, August 29, 2020.

60 Scott Shane, "Researcher in Isolation Appears Healthy Despite Possible Ebola Exposure," *The Baltimore Sun*, February 21, 2004.

scientist named Patrick Iversen, who would later work closely with the CBDP, was called.[61] That day he had made a presentation on rapid creation of therapeutics based on a pathogen's genetic material. The FDA gave emergency approval of a synthesized drug created by Iversen in two days. Although the researcher was not in the end infected, the turnaround impressed defense leaders, and some of Iversen's research was funded as part of the Transformational Medical Technologies Program mentioned above, an early effort to rapidly create medical countermeasures against biological weapons.

The Transformational Medical Technologies Program and larger CBDP efforts that followed have had success in shifting the DoD toward faster, more flexible, and more cost-effective responses to biological threats. For instance, after aiding in the response to the lab accident described above, this rapid-response approach was used to create a therapeutic during the Swine Flu pandemic of 2009.[62]

Based on an analysis of CBDP budgets over the last four years, funding for these types of technologies---colloquially referred to as rapid response platforms---appears to be consistently on the rise.[63] Today, examples of ongoing programs include novel vaccine development approaches and continued funding for an advanced facility that is currently being used to manufacture a nucleic-acid-based vaccine against COVID-19. The facility has also been configured to manufacture treatments against botulinum toxin, an upgrade over the DoD's single-horse source of botulinum antitoxin prior to the first Gulf War.[64] In addition, the program is investing in hypothesis-free detection methods that are necessary against novel biological threats of all types, such as sequence-based diagnostic tests.[65]

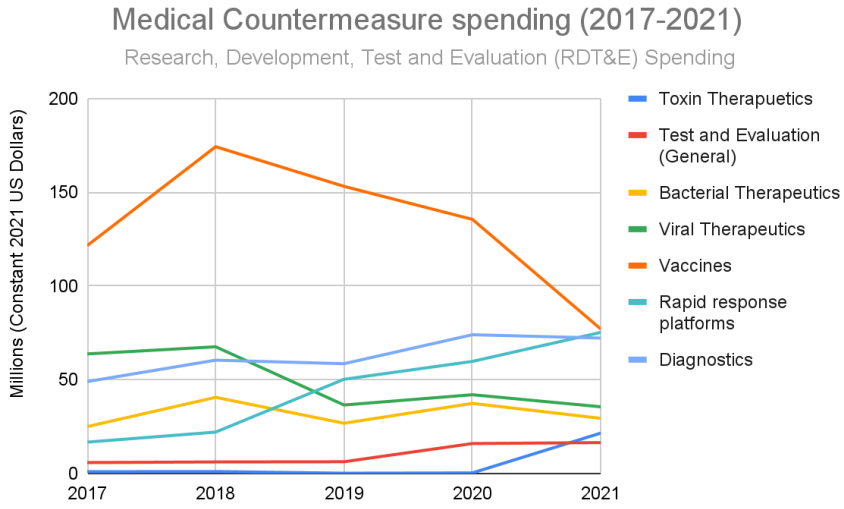

Figure 1: Comparison of RDT&E spending on medical countermeasures at CBDP, 2017-2021[66]

61 Thomas H. Maugh II, "Drugs Block Ebola, Marburg Viruses in Tests," *Los Angeles Times*, August 23, 2010.

62 Julie Rathbun, "AVI BioPharma, Inc. Under Contract With U.S. Defense Threat Reduction Agency for Development of Therapeutics Targeting H1N1 Swine Flu," *BioSpace,* June 22, 2009.

63 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission" (Washington, DC, 2016-2020). Please note that the data collected is based on a review of DoD budget documents at the source above, with particular attention paid to the research, development, test and evaluation submissions for the CBDP from 2017-2021.

64 Hannah Feldman, Chris Earnhart, and Traci Pals, "Toxic at Best," *U.S. Department of Defense, JPEO-CBRND,* January 22, 2019.

65 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2021 Program and Budget Review Submission," 2020.

66 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission" (Washington, DC, 2016-2020). Please note that the data collected is based on a review of DoD budget documents at the source above, with particular attention paid to the research, development, test and evaluation submissions for the CBDP from 2017-2021.

The creation of the CBDP has been incredibly important to the safety of defense forces and to global health security. However, similar to the state of U.S. biological defense in the past, CBDP's funding has diminished in recent years. These trends, described next, must be reversed.

CRITICAL WORK YET DECLINING RESOURCES

Biological threats are rising. Unfortunately, many aspects of CBDP's budgets are trending in the opposite direction. During the most consequential biological event of our lifetimes, the COVID-19 pandemic, the CBDP's budget was reduced. Over the last decade, the CBDP's budget (in constant 2021 U.S. dollars) has trended consistently downwards.

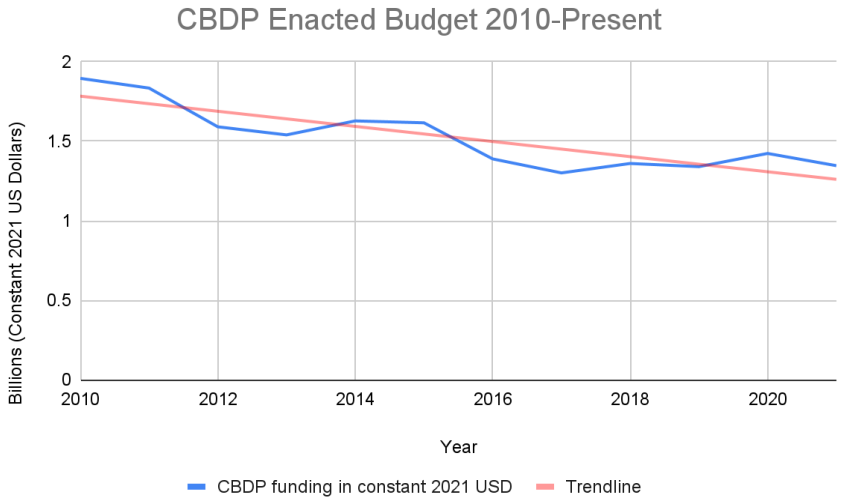

Figure 2: CBDP spending from Fiscal Year 2010-2021[67]

67 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2010-2021 Program and Budget Review Submission" (Washington, DC, 2020). The chart is based on the authors' review of approximately 20 DoD budget documents at the source above, including both procurement and research, development, test and evaluation submissions for the CBDP for all years; U.S. Congress, Senate, Committee on Appropriations, "Congress Reaches Deal, Files FY21 Omnibus to Fund Govt, Provide COVID Relief, Joint Explanatory Statement C," 116 Cong., 2nd sess., 2020. To ensure the enacted budget was included for 2021, the Congressional appropriations explanatory document was referenced.

As can be seen in Figure 3 below, since the 2005-2010 average, the budget has been reduced by almost one third.

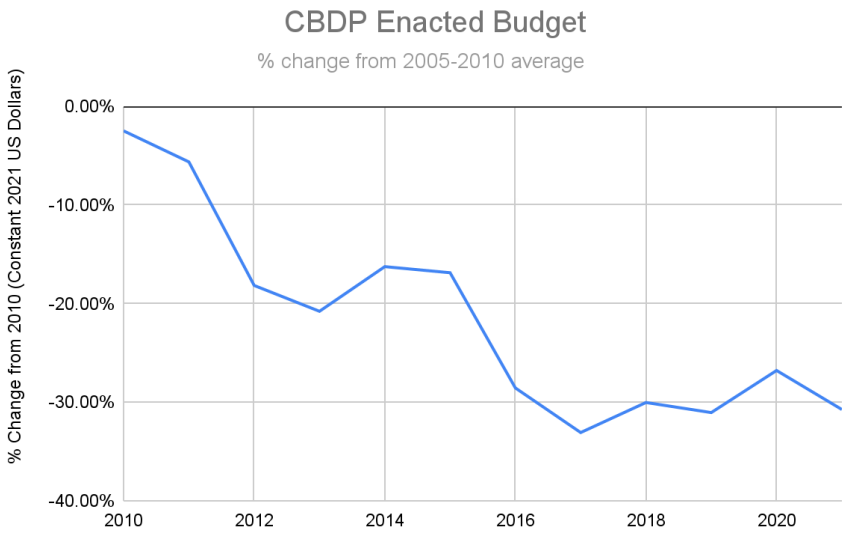

Figure 3: CBDP annual budgets 2010-2021, compared to the program's 2005-2010 average annual spending[68]

These budgets cover work to counter both biological and chemical threats, but reductions are coming mostly at the expense of countering biological threats. Biological defense spending has been on a consistent downswing since 2014, while chemical defense spending has been trending upwards. This is a significant problem, and in 2020 it caught the attention of Senators Mitt Romney and Mike Lee, who introduced an amendment requiring DoD to report on how cuts to the CBDP will have an effect on national security.[69]

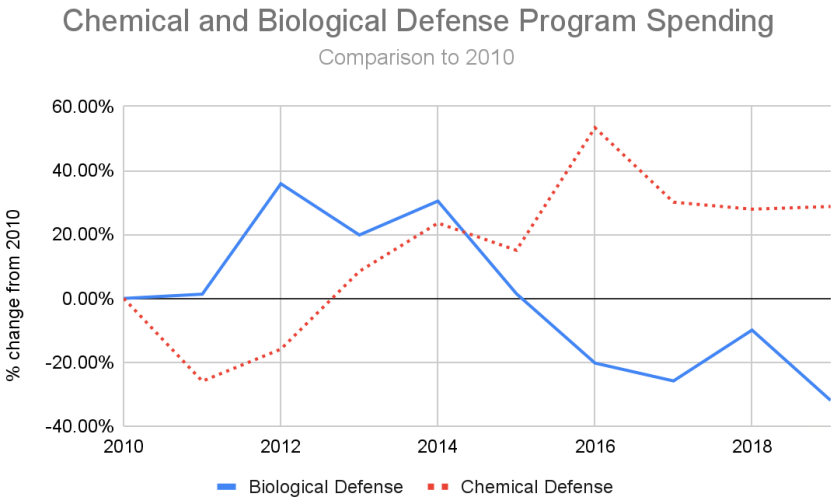

Figure 4: Percentage change from 2010 CBDP spending in biological and chemical defense spending.[70]

68 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission." The data is based on the authors' review of approximately 30 DoD budget documents at the source above, in particular the procurement and research, Development, test and evaluation submissions for the CBDP from 2005-2021.

69 The Office of U.S. Senator for Utah Mike Lee, "Senate Passes NDAA With Lee-Backed Amendments," July 23, 2020.

70 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Years 2010-2018 Program and Budget Review Submission" (Washington, DC, 2010-2018).

As has been observed in the Syrian government's use of chemical weapons and Russia's application of Novichok nerve agents for assassinations, chemical weapons remain a real threat. However, biological weapons are also a serious threat that many experts believe will become - worryingly - more attractive in the years ahead. There are a range of scenarios in which biological weapons may be used and for which U.S. forces need to be prepared. Anthrax, for example, could be used in a targeted manner against specific populations or forces, a large-scale attack, and everything in between. They may also be considered for anti-access/area denial, or preventing another nation's forces from operating in a specific area. The DoD is beginning to prepare for such a risk, as seen in its conduct of an exercise in the fall of 2020 in which the scenario began with a Chinese biological weapon attack on U.S. bases and warships in the Indo-Pacific region.[71]

There are reasons that countries would favor a biological weapon like anthrax, including the major effects that can be achieved with small quantities. The Office of Technology Assessment of the U.S. Congress estimated that 100kg of anthrax released over Washington, DC could lead to 130,000 to 3 million deaths, similar in lethality to a hydrogen bomb.[72] Beyond operational applications, biological weapons have been viewed as strategic-level weapons. The Soviet Union weaponized smallpox and conducted tests to prepare to use it against U.S. cities and civilian populations in the event of an all-out nuclear war.[73] Countries such as North Korea may also see utility in the deniability that biological weapons can bring.

Despite these threats and many more, biodefense investment is trending downwards in high-priority areas. For the Fiscal Year 2021 U.S. President's Budget Request, significant cuts to vaccine-related activities were originally proposed.[74] These reductions were partially restored in a last minute legislative maneuver in Congress in December 2020.[75] However, there are concerns that similar cuts will be proposed again in future defense budgets. The effects of cuts in vaccine investments in and of themselves might be mitigated if the funding was then transferred to rapid response platforms. However, instead, the trend is that funds are shifted out of the CBDP altogether.

In addition, tools used to inform the DoD about biological threats and aid in decision-making are being cut. Most of these reductions are coming from the data and software backbone of capabilities to collect and share biothreat information.[76] The importance of situational awareness for biological threats has become clear during the pandemic. The early 2020 COVID-19 cases among the crew of the *USS Theodore Roosevelt* aircraft carrier stemmed from the ship entering port in Vietnam during the pandemic---shore leave for the crew that included a 400-person reception---out of a belief that the country was low risk.[77]

The CBDP has significant capabilities that can be used for pandemic detection and response. Yet during the COVID-19 pandemic, which clearly required an all-hands approach, CBDP's funding was reduced. There were

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71 James Kitfield, "'We're Going to Lose Fast': U.S. Air Force Held a War Game that Started with a Chinese Biological Attack," *Yahoo News,* March 10, 2021.

72 Office of Technology Assessment, *Proliferation of Weapons of Mass Destruction: Assessing the Risks* (Washington DC: U.S. Government Printing Office, 1993): p. 54.

73 David McGlinchey, "Soviet Union Once Deployed Smallpox-Tipped ICBMs," Nuclear Threat Initiative, October 22, 2003.

74 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "Department of Defense Fiscal Year (FY) 2021 Budget Estimates - Chemical and Biological Defense Program, Defense-Wide Justification Book Volume 4 of 5," 2020.

75 U.S. Congress, Senate Committee on Appropriations, "Congress Reaches Deal, Files FY21 Omnibus to Fund Govt, Provide COVID Relief, Joint Explanatory Statement C," 2020.

76 Please see U.S. Department of Defense, Under Secretary of Defense (Comptroller), "Department of Defense Fiscal Year (FY) 2021 Budget Estimates - Chemical and Biological Defense Program, Defense-Wide Justification Book Volume 4 of 5," 2020 and U.S. Congress, Senate, Committee on Appropriations, "Congress Reaches Deal, Files FY21 Omnibus to Fund Govt, Provide COVID Relief, Joint Explanatory Statement C," 2020.

77 "Timeline: Theodore Roosevelt COVID-19 Outbreak Investigation," *U.S. Naval Institute News*, June 23, 2020.

opportunities for the CBDP to receive funding through emergency spending bills in response to the pandemic, but DoD was hesitant to request further funding because of confusing guidance from the Secretary of Defense and uncertainty within the DoD around the use of CBDP resources against a pandemic that did not stem from biological weapons. Secretary of Defense Mark Esper's *Defense Wide Review* in late 2019 slashed the CBDP top line nearly 10 percent and the medical biodefense component by one-third. This worsened an already long cycle of neglect against biological threats, including a halt in the above-mentioned biological threat exercises with the Republic of Korea.

Weaknesses in the U.S. response to COVID-19 may also perversely incentivize nations that may be interested in biological weapons to hedge more toward latent capabilities to create them, or worse. The effects of infectious disease threats on the American people, economy, and national security are clear. Restoring and augmenting the CBDP's budget is one of many critical steps to strengthen U.S. defenses against these threats---and with the same work, signal to potential adversaries that any future use of pathogens as weapons will be ineffective at causing mass destruction.

In one of the most worrisome issues of the U.S. COVID-19 pandemic response, CBDP's potential contributions were limited and at times altogether disallowed. This stemmed from disagreements within the DoD on whether the CBDP should be involved in responding to natural infectious disease outbreaks.[78] This instruction is especially unhelpful given that a deliberate biological attack may appear to be a naturally-occurring outbreak. The lack of clarity around this question has real consequences. As we have seen, the CBDP has played critical roles in the response to the Swine Flu pandemic of 2009 and the Ebola outbreak that began in 2013. CBDP could have contributed similarly in the COVID-19 response. Instead, U.S. government assets developed over years to counter biological threats were left unused as Americans died.

RECOMMENDATIONS

The CBDP's mission is difficult: to research, develop, and deploy assets, equipment, and technologies against biological threats that could impact force performance in specific regions and across the globe. This mission is becoming more difficult with time as the biological threat space grows larger on all three dimensions: natural, accidental, and deliberate.

The DoD biodefense community, CBDP and DARPA in particular, have shown an ability to make game-changing contributions to U.S. efforts against biological threats. This work, especially when focused on versatile technologies that are both maximally useful against engineered biological weapons and helpful against novel emerging infectious diseases and other biological threats, has significant potential.

CBDP investment now in technologies against biological threats can allow the United States to get ahead of these threats and create strong defenses. Increasing the CBDP medical biological defense budget will also augment its ability to leverage national assets that have been built over decades of investment. Put simply, this work is crucial to U.S. national security and the health security of every American. As such, we recommend the following steps.

The President's next budget request should roughly double CBDP funding to at least $2 billion and be increased to the $6.5 billion to $7 billion annual budget range by the end of the decade.

This resource level, which should be held consistent and adjusted for inflation over time, is required to show

78 U.S. Department of Defense, Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs, "CBD Mission."

that the nation is serious about addressing biological threats and is robustly increasing its capabilities in this area. This investment should of course be coupled with substantial, complementary increases in budgets for HHS, the Departments of Energy and State, and other components of the U.S. ecosystem for defending against biological threats. These resources will also encourage innovation in the U.S. economy.

Most of this increase should focus on biological threats, including restoring significant funding to CBDP's unique capabilities regarding medical countermeasure development and international partnership activities. There is some overlap between capabilities for countering biological and chemical threats, but it is clear that a substantial topline budget increase is required to meet national security needs against biological threats without cutting into equally-important work against chemical weapons threats.

These additional resources are also required in order for DoD to take full advantage of the fact that the world is on the cusp of bringing game-changing technologies to the fight against biological threats. Breakthroughs in the biological sciences, combined with those in robotics, machine learning and AI, advanced manufacturing capabilities, and others have positioned the United States and its partners around the world to drive a new era in more rapidly and effectively countering infectious disease threats. The United States should absolutely seek to be the world leader in bringing these advances fully to market, and in using them to meet national security needs. The CBDP is already ideally positioned to play a central role in this.

One function of these resources should be to meet a goal of advancing new medical countermeasures to FDA approval and licensure. The CBDP has already invested significantly in research and development for many countermeasures that may be needed against disease threats to U.S. forces (and which may have substantial benefit for public health as well). For all promising medical countermeasures, DoD should be capitalizing on these past investments.

With its unique range of research and development work, as well as significant testing and evaluation capacities, the CBDP should develop a plan and seek resources to execute an annual program to exercise its capabilities for rapidly developing new diagnostics, medical countermeasures, and more (as described in *Part VI* of this report). This can be done in coordination with other government agencies, and eventually also with international partners. The COVID-19 pandemic has shown that fast development and fielding of diagnostic tests, vaccines, and therapeutics can make the difference in being able to contain an infectious disease outbreak. If a biological threat, possibly an engineered one, is deliberately introduced, the effects on the public and U.S. forces may be far beyond the effects of the current pandemic. Showcasing rapid response capabilities---especially doing so every year---will also help deter adversaries from considering development and use of biological weapons.

Rapid response platform technologies, such as those used to create some types of COVID-19 vaccines, should naturally be a component of such a development and testing program. Additional priorities may include:

- Building additional "Advanced Development and Manufacturing" facilities that are versatile and can be used for rapidly responding to a biological weapons attack or infectious disease outbreak. Ideally, this infrastructure will be kept warm by being used in exercises or in responding to natural disease outbreaks or even seasonal influenza.
- Investing in development of hand-held, user-friendly metagenomic sequencing technologies that can be used in the field or clinic to detect biological weapons or emerging infectious diseases.
- Leaning into the promise of nucleic acid-based therapeutics, which should continue to receive the investments needed to fully advance them to potential use authorization.

- Developing next generation personal protective equipment that is more effective against viruses. The technology is here to create masks far superior to N95s and specifically targeted against viruses and bacteria.
- Researching sterilization and pathogen transmission suppression within buildings, planes and ships, a key issue during both a pandemic and biological weapons attack.
- Developing point-of-person diagnostic platforms to be used routinely in the field.
- Continuing broad-spectrum, small-molecule antiviral research.

Many of these funding areas were also recommended in the Bipartisan Commission on Biodefense's 2021 report *The Apollo Program for Biodefense – Winning the Race Against Biological Threats*.[79] This increase in funding can help incentivize the private sector to view the DoD as a more attractive partner. However, the funding must be maintained over the longer term to ensure it makes sense as a business case for private sector partners, and it will require Congress and the DoD to work closely together.

Leadership in both Congress and the DoD (especially the Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs and the Office of the Secretary of the Army) will be needed in ensuring that funding remains at this level.

The Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs (ASD(NCB)), in cooperation with the Secretary of the Army and others, should rejuvenate DoD's leadership against biological threats.

For the vast majority of the last seven years as of this writing, the ASD(NCB) role has been filled by an acting official who was neither presidentially appointed nor Senate confirmed. This can result in a dynamic where the acting official's top cover and self assurance to enact change are limited.[80] As a result, a significant leadership void has opened in DoD efforts to address biological threats, including on how to appropriately and effectively leverage assets like CBDP to contribute to national responses against the COVID-19 pandemic. The administration and Congress should work to ensure this does not happen again.

In addition to showing personal support for the CBDP enterprise and fighting for the above-listed sufficient resources, specific actions should include the following:

Coordinate with the DARPA director. Many technologies of high potential have come from the Defense Advanced Research Projects Agency (DARPA). Because of its relatively flat structure and deliberate frequent personnel changes, DARPA often spots and encourages development of new, high-potential technologies more easily than other DoD organizations. The CBDP is already working with DARPA on transitioning many technologies to use in the military.[81] However, more direct cooperation and simultaneous exploration of technologies should be considered as a form of healthy competition and a means to increase investment in these important areas. The ASD(NCB), DARPA Director, and Secretary of the Army could begin expanding collaboration with a joint meeting among them to set some priorities and general vision, followed by memos to their respective staffs with implementation instructions regarding those high-level goals and priorities.

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79 Bipartisan Commission on Biodefense, *The Apollo Program for Biodefense: Winning the Race Against Biological Threats. Bipartisan Commission on Biodefense* (Washington DC: Bipartisan Commission on Biodefense, 2021): pp. 11 - 25.

80 Russell Berman, "President Trump's 'Substitute Teacher' Problem," *The Atlantic,* April 26, 2017.

81 Amber Kriesel, *U.S. Department of Defense, JPEO-CBRND,*"DARPA and JPEO-CBRND Formalize Collaborative Efforts to Support American Military Personnel," December 13, 2018.

Be a good consumer of biological threat intelligence---and be sure that other senior DoD leaders are too. Senior leaders that oversee most of DoD's investments against biological threats should help create a demand signal for strong intelligence in this space. Perhaps just as importantly, they should ensure that key intelligence is provided to defense leaders who need to understand the threat when making budget and leadership decisions, such as the Secretary and Deputy Secretary, all relevant Under Secretaries, Service Secretaries, and the Commander of Special Operations Command. After the COVID-19 pandemic, it will be important to keep a close watch on potential efforts by state and non-state actors to develop or hedge toward biological weapons. In addition, more generally, intelligence briefings will aid in investment decisions.

Direct the Deputy Assistant Secretary of Defense for Chemical and Biological Defense to organize additional annual exercises with partners. In cooperation with intragovernmental, private sector, and international partners, the CBDP should conduct annual exercises to test its early warning capabilities for novel pathogens and rapid responses. This will regularize cooperation between the CBDP and its partners, increase deterrence against adversaries considering developing or using biological weapons, and also help ensure that the United States and the world are prepared for the next high-consequence biological threat.

Broaden international cooperation to include identifying opportunities for technology development and sharing with allies and partners. As described above, regular discussion and cooperation with allies and partners is an important way to augment capabilities. Depending on its sensitivities, the CBDP can also help identify some technologies and tools that may be shared or sold to key partners. This cooperation may also make an important contribution to deterrence.

Senior DoD leaders should broaden the mission of the CBDP in high-level documents to extend beyond ensuring continuity of military operations in the case of biological and chemical weapons being used against defense forces.

First and foremost, those volunteering to defend the United States deserve technologies that help them avoid the risk of operating in such environments as part of their military missions---not just protective gear that may be needed for such operations.

Second, in many potential conflict environments, protecting military families and embassy staffs, and preventing mass-casualty events among the public, should be seen as mission support as well.

Third, the CBDP's work should be explicitly recognized for its contributions to deterrence. Indeed, a mission of the CBDP should be to deter biological attacks against the United States, its allies and partners. It is clear that biological threats pose a significant strategic threat. As part of whole-of-nation preparedness to mitigate this threat, CBDP investments for DoD that at the same time benefit the American public writ large should be explicitly recognized and encouraged. As stated above, it is quite possible that early in the use of a biological weapon, the distinction of whether it is of natural or deliberate origin may remain ambiguous. The CBDP's contributions to the nation's effective responses should never again be constrained by lack of clarity on its scope of mission.

The ASD(NCB) should also direct the Deputy Assistant Secretary of Defense (DASD) for Chemical and Biological Defense to confer with DoD lawyers to get a clear decision on any perceived limitations on CBDP authorities regarding its mission scope, if they exist. Future Congressional acts may also explicitly state that CBDP funds can be used against the full range of biological threats, to include potential pandemic pathogens, in order to avoid potentially critical assets being left on the shelf during biological crises because of definitional issues regarding deliberate, accidental, and natural

biological threats. This should be part of a continued shift away from the outdated approach of developing technologies based on a specific, relatively static list of pathogens (the Select Agents List) viewed as having potential as a bioweapon.

DoD should set a process for balancing risk and reward, including consideration of dual-use risks, and to consider measures to increase transparency.

Increased investment in biodefense runs the risk of causing concern among allies and adversaries about the character of DoD intentions. It is important to ensure that technologies are chosen that have a clear intention and application for defensive purposes only. Transparency measures, including confidence-building efforts with third-party states, can increase transparency while not sacrificing national security.

Organizations such as the Intelligence Advanced Research Projects Activity (IARPA) have, in the past, had particularly forward-thinking review processes of this type in place that should be considered when making decisions about programs to fund. As funding is being restored to the CBDP, it will be important to ensure that additional activity does not give rise to misunderstandings about the defensive nature of its work. Red-teaming ideas with experts from the National Labs, Department of State, and health and intelligence agencies could help in that regard.

CONCLUSION

There is a growing gap in U.S. biodefense that is making the country as a whole, including the U.S. military, more vulnerable. This has become apparent during the COVID-19 crisis, the largest biological incident of our lifetimes. A substantial increase in CBDP investments, together with the shifts in CBDP activities outlined above, will help shore up U.S. biodefense and rapid response capacities, and better protect the nation in the present time and the coming decades against catastrophic biological risks.

Various federal agencies have specific authorities and mechanisms for addressing threats and emerging needs quickly. Still others are designed to give the federal government more agility and flexibility in how they seek to foster or purchase cutting-edge technologies. Examples that should be leveraged to advance U.S. capabilities for addressing catastrophic biological risks include:

Other Transaction Authorities (OTAs). The Department of Defense (DoD) has authorities to conduct "other transactions" beyond normal contract and acquisition processes for both research and prototype work.[82] OTAs have become a critical tool for the department accessing more advanced technologies, in particular with smaller and more innovative companies.

JUONS and JEONS processes. Elements in the Department of Defense can create Joint Urgent Operational Need (JUONs) and Joint Emergent Operational Need (JEONs) statements that indicate (respectively) that a capability gap exists that needs to be filled as quickly as possible, or that an emerging operational need is becoming clear and should be met with solutions.[83] COVID-19 showed how greatly disease threats can affect defense forces, and how swiftly they can hit. As such, DoD may benefit from using these mechanisms in the near term to quickly adopt better technologies for addressing them.

Co-mingling Authority. After 9/11, what was then the G8 group of nations formed the Global Partnership for Countering WMD to coordinate multiple countries' investments in addressing WMD threats. Given the U.S. Department of Defense's extensive capacities, relationships, and contract mechanisms, interest rose in the Cooperative Threat Reduction Program accepting funding from Global Partnership nations to "co-mingle" with U.S. funds to ramp up important work. This has become a unique and flexible way to operate, including in fast responses to emerging threats, and should be regularly put to use for addressing biological threats.

Multi-year and Moveable Funding. The Cooperative Threat Reduction Program normally features annual authorizations of multi-year funds (e.g., the ability to spend funds over up to 3 years, rather than in a single calendar year) and limited discretion of the Department of Defense to be able to move dollars across specific areas of the program. More government programs should enjoy similar authorities given the flexibility this provides to respond to threats within a specific program or agency's mission. However, U.S. Congress and Executive Branch leaders must be vigilant each year to ensure that these authorities are not used to diminish investments against biological threats, for example by moving Biological Threat Reduction Program funds to efforts to address nuclear threats.

These are just a few examples of unique authorities that staff working on solutions to biological threats should use as often as is appropriate. Senior leaders in bio-relevant positions should also instruct their staff to remain prepared to seize opportunities to use these mechanisms, and provide the relevant acquisition training to relevant personnel to help empower them to do so.

82 U.S. Department of Defense - Defense Acquisition University, "Contracting Cone: Other Transactions (OT)," 2018.

83 U.S. Department of Defense - Defense Acquisition University, "Types of Urgent Operational Needs (UONs)," 2015.

Andrew Weber carries a piece of equipment at a former Soviet biological weapons facility in the northern Kazakhstan town of Stepnogorsk in this July 25, 2000 file photo. The Biological Threat Reduction Program demilitarized the facility and prepared it for demolition. Andy Weber/National Security Archive

THE BIOLOGICAL THREAT REDUCTION PROGRAM[84]

The first case of COVID-19 identified outside of China occurred on January 13, 2020, in Thailand. This early detection can in large part be credited to a little-known yet essential U.S. Department of Defense (DoD) program, the Biological Threat Reduction Program (BTRP), which equipped partners in Thailand with disease surveillance technologies and trained experts on their use.[85]

This is just one of countless examples of the BTRP's successes stemming back to the immediate post-Cold War years, when the program helped guide the world through one of the more tumultuous periods of technology-related risk in modern history.

Between 1972 and 1991, the Soviet Union amassed the largest biological weapons stockpile in history---sufficient to end all life on Earth. This included an annual production capacity for weaponizing smallpox that grew to two tons by

84 Much of the text in this section is drawn directly from Bill Beaver, Christine Parthemore and Nikki Teran, "Key U.S. Initiatives for Addressing Biological Threats Part 3: The Biological Threat Reduction Program," Council on Strategic Risks, August 9, 2021.

85 Andrea Chaney, Office of the Deputy Assistant Secretary of the Army for Defense Exports and Cooperation, "Strong International Relationships Enabled DTRA to Provide COVID-19 Support to Partners Abroad," February 2, 2021.

1990. Smallpox kills thirty percent of those infected and spreads just as easily as SARS-CoV-2.[86] The Soviet program included up to 65,000 employees in 50 to 60 facilities.[87] Then, in 1991, the Soviet Union disbanded. The weapons, equipment, facilities, raw materials, and people involved in this program became one of the top weapons of mass destruction risks in the world. The United States stepped in and worked hand-in-hand with Soviet successor states to keep countries such as Iran from inheriting Soviet biological weapons capabilities. Originally called the Cooperative Biological Engagement Program, BTRP work helped to destroy these biological weapons facilities, secure dangerous pathogens, and put experts to work in peaceful pursuits.

BTRP has grown and changed over its approximately twenty-five years of protecting the world from biological threats, and it must be resourced and led to continue evolving as biological threats do. The scale, geographic spread, and irresponsibility of the activities of the Soviet biological weapons program were an intimidating problem. More recently, the continuous growth in the number of high-containment research labs throughout the world, including but not limited to China, poses similar biosafety and security problems. Dangerous activities such as gain-of-function research and efforts to discover new viruses from nature pose dangerous pandemic and potentially biological weapons threats, even if they may provide some public health benefits. Developments in biotechnology are making it easier for actors to engineer biological weapons. Viruses or bacteria engineered to slip by existing pathogen early warning systems and countermeasures are well within reach of the majority of countries today and are a serious potential asymmetric threat to U.S. and allied forces.

Fully leveraging the historic BTRP program and all the assets it holds will require a realignment of resources and policy instruction. BTRP enjoys the support of several cross-party Congressional champions. White House guidance in April 2021 indicated that top DoD priorities should include "biological threat reduction in cooperation with global partners, emerging infectious disease surveillance, biosafety and biosecurity, and medical countermeasure research and development."[88] BTRP is one of the core programs for advancing such work. Yet in the final administration budget submitted to Congress for the upcoming fiscal year, FY22, BTRP funding was slashed by 45% from the prior year.[89]

As a cornerstone program for addressing biological threats, this section provides several recommendations to help ensure the BTRP is sufficiently robust and effective in the coming years. It concludes by recommending that BTRP resources be increased to up to $400 million per year, a level of effort more commensurate with the threats the program addresses and sufficient to position BTRP as a key contributor to the U.S. bioeconomy as a strategic asset of the nation.

MAXIMIZE BTRP'S LONG-TERM CONTRIBUTIONS TO U.S. SECURITY STRATEGY

It is in the strategic interest of the United States to be the most attractive partner for countries seeking cooperation and support in enhancing their capacities to mitigate biological threats. If the United States does not play this role, other countries will likely do so, including Russia and China.

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86 Please see Milton Leitenberg, Raymond A. Zilinskas, and Jens H. Kuhn, *The Soviet Biological Weapons Program* (Cambridge, MA: Harvard University Press, 2012); Donald A. Henderson, "The Eradication of Smallpox – An Overview of the Past, Present, and Future," *Vaccine* Vol. 29, Suppl. 4, 2011: pp. D7-D9; and Ron Sender, Yinon M. Bar-On, Shmuel Gleizer, Biana Bernshtein, Avi Flamholz, Rob Phillips, and Ron Milo, "The Total Number and Mass of SARS-CoV-2 Virions," *Proceedings of the National Academy of Sciences* Vol. 118, No. 25, 2021: pp. 1 - 9.

87 Leitenberg et al., *The Soviet Biological Weapons Program.*

88 U.S. White House, Letter to the Senate, "Summary of the President's Discretionary Funding Request," April 9, 2021.

89 Department of Defense, Office of the Undersecretary of Defense (Comptroller), "Fiscal Year 2022 President's Budget: Cooperative Threat Reduction Program," 2021.

Russia and China in particular target audiences in Central Asia, Southeast Asia, the Middle East, Africa, and elsewhere to cast their respective nations as an ideal partner. This can generally have a negative effect on U.S. interests. It increases the odds of such nations adopting norms that may not align with those of the United States. In concrete terms, it also means that audiences in these regions receive misinformation conveyed by these nations---for example, Russian accusations that U.S. threat reduction programs are hiding bioweapons activities, and Chinese misinformation surrounding COVID-19. The long-term trust produced through BTRP and other bio cooperation programs is critical for countering this.

In many cases, trust-building requires sustaining relationships and cooperative efforts over the long term, just as BTRP has facilitated partnerships with former Soviet states such as Kazakhstan and Georgia for decades. Yet in recent years, the Defense Threat Reduction Agency (DTRA), which implements the program, has faced pressure to build capacity and then mostly exit countries with which it has invested. These nations take on more programmatic responsibility over time (e.g., sustainment costs for laboratories and personnel), yet too-steep reductions in U.S. presence would undercut the U.S. ability to understand Russia's behavior in the region and effectively deter Russian aggression. Via persistent, long-term cooperative partnerships, BTRP both directly reduces biological risks and supports broader U.S. security imperatives.

While partner nations need to bring their own resources to sustaining capabilities so that U.S. contributions can shrink over time, maintaining relationships built and awareness of the bio activities of these partners is invaluable for the United States. Given that biological threats grow exponentially and spread across borders, close, consistent relationships allow the United States far better early knowledge of emerging biological threats that can inform DoD and the nation in implementing appropriate precautions and mitigation strategies---for example, developing and deploying diagnostic tests for specific pathogens around U.S. bases and embassies.

Ensuring high-level Executive Branch and Congressional support for BTRP will require that key leaders regularly and effectively communicate how this program helps to enact U.S. strategy on the ground in important regions. For example, those in positions like the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs and the DTRA Director can help ensure this work is tied into the national security strategy, and continually inform the highest-level defense leaders about the importance of these programs to help increase support for strong budgets during annual planning cycles. Too often, defense and diplomatic leaders with regional focuses are unaware of how functional programs like BTRP can support their goals. It is incumbent on BTRP leaders and those that oversee the program to communicate its benefits effectively to these audiences.

BTRP strengthens ties to key partners and allies and enhances the U.S. position vis-a-vis countries like Russia and China, in addition to directly mitigating biological threats. The program also directly helps to protect U.S. forces, allies, and the public. The following, specific areas of effort all support these national goals.

REDUCE GAPS AT HIGH-RISK HOTSPOTS

Governments in many countries lack strong, central knowledge of what researchers may be doing with especially dangerous pathogens within their own borders. Until recently, there was no public accounting of high-containment labs (those designated at biosafety levels 3 and 4) dealing with dangerous pathogens globally, though such labs

Former Soviet biological weapons test site at Vozrozhdeniye Island. The contaminated site presented a growing threat because the shrinking of the Aral Sea resulted in increased human and animal access to the formerly isolated islands, as well as the potential that contaminated dust could eventually blow across to the mainland. The Biological Threat Reduction Program (BTRP) dismantled dual-use equipment, technologies, and associated infrastructure. BTRP excavated and destroyed live pathogenic material (B. anthracis) with zero incidents of release, exposure, or contamination at a remote location. Andrea Chaney/Defense Threat Reduction Agency

have proliferated in number recently.[90] BTRP's work includes promoting consolidation of dangerous pathogens at such labs and training their personnel to improve safety and security. This should be one of the top priorities of the Department of Defense and the U.S. government more broadly.

BTRP should focus additional resources on high-risk hotspots like high-containment laboratories in the years ahead. The U.S. intelligence community's continuing low level of certainty regarding whether COVID-19 was initiated naturally or via a lab accident from a facility conducting work on the pathogen shows the critical importance of work to reduce the risks of such accidents.

Cooperative biosafety and biosecurity activities can have the added benefit of increasing transparency regarding countries' biodefense programs. The Biological and Toxin Weapons Convention (BWC) does not effectively distinguish between allowable biodefense activities and prohibited bioweapons work, making insights from programs like BTRP regarding the nature and intention of bio work conducted around the world invaluable.

90 Filippa Lentzos and Gregory Koblentz, "Mapping Maximum Biological Containment Labs Globally," King's College London, May 2021.

LEVERAGE BTRP TO ADVANCE PATHOGEN EARLY WARNING

One of the great successes of BTRP to date has been in building biosurveillance capacity with key partner nations around the world---including those proximate to nations for which the United States is concerned about biological weapons activities such as North Korea and Russia.[91] BTRP is therefore ideally positioned to help implement the vision coalescing across the international community of transforming biosurveillance (by which disease threats are often detected and tracked days, weeks, or longer after they emerge) into a real-time pathogen early warning system.

Implementation will entail a wider use of tools like next-generation genomic sequencing (especially metagenomic sequencing) which can help in finding and characterizing a vast range of pathogens within hours, coupled with big-data analytics and machine learning systems that can rapidly warn of potential emerging threats. This could significantly increase global capacity for halting natural outbreaks. Yet some of its greatest promise is for quickly identifying deliberately-introduced biological threats. Pathogen early warning tools, including those that have just come into use in the past few years, offer incredible promise against biological weapons---think, for example, of the benefit to further improving pathogen early warning in South Korea, where tens of thousands of U.S. defense personnel and their families reside and for which the stakes for understanding an outbreak fast are incredibly high. Indeed, such systems can be an effective deterrent against the development and use of biological weapons.

Not all of today's biosurveillance capabilities are useful in detecting the signs of a biological event that may stem from a deliberate attack or involve engineered pathogens. Some are slower than is helpful in terms of keeping defense forces safe. Others are capable of only detecting specific, known pathogens and are not useful for novel diseases.

One of the most important ways in which BTRP should expand in the coming years is in building on its rich history of collaboration and trusted relationships around the world to deploy cutting-edge early warning capabilities that will be maximally useful in catching and characterizing deliberate biological threats and new, novel pathogens that may pose serious risks to personnel. As technologies such as metagenomic sequencing are deployed more broadly, BTRP should be at the forefront of providing them to existing and new partners and ensuring training for their use, as it has done with longer-standing genomic surveillance approaches with partners in the former Soviet Union, Southeast Asia, and elsewhere.[92]

EXPAND BTRP AUTHORITIES & EXERCISE THEM MAXIMALLY

One of the most important aspects of BTRP is that the program is designed with flexibility to either perform its work directly or to fund other, non-defense entities to execute projects, depending on what is best for each threat reduction circumstance. Given the sensitive nature of biological threats and solutions, at times progress with a specific country or laboratory is most likely via universities, nongovernmental organizations, or the U.S. Centers for Disease Control and Prevention (CDC). In other cases, having a defense agency presence at the forefront is best.

Various BTRP authorities, as well as its collaboration with non-defense agencies, also help provide significant insights for understanding how potential biological weapons threats may manifest and how nefarious actors may misuse synthetic biology in the future, and otherwise improve defense force health protection.

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91 U.S. Department of State, "Adherence and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments," 2019: pp. 45 - 50.

92 The technologies discussed in our briefer "Pathogen Early Warning: New Technologies and Approaches" would enable a biological weapons early warning system that is so difficult to engineer around that it would be a key capability that significantly deters countries from developing or releasing biological weapons.

In Sierra Leone, the Biological Threat Reduction Program (BTRP) provided and provisioned a Mobile Diagnostic Laboratory to help stem the largest outbreak of Ebola in history in 2014. Andrea Chaney/Defense Threat Reduction Agency

Several examples stem from work on orthopoxviruses, which are highly concerning given their presence in the former Soviet Union's biological weapons programs, the focus on these viruses by other nations, and recent trends in experimenting with them. In 2018, Canadian scientists published an article based on work to synthesize horsepox virus, further raising concerns regarding nefarious actors synthesizing the Variola virus which causes smallpox.[93] Human monkeypox is also rising in parts of Africa where it is endemic and which coincides with areas of longstanding conflict. Symptoms of patients ill with monkeypox are nearly clinically indistinguishable from smallpox. Partnerships in Africa have allowed DoD to understand trends related to monkeypox rising and mutating---insights useful to understanding potential smallpox threats as well.[94]

BTRP's ability to work with diverse partners directly provides windows into trends in this genus of viruses, and also allows the defense community to find efficiencies in solutions based on such knowledge. For example, the deployment of genomic sequencing in key parts of Africa has facilitated our understanding of how the smallpox vaccine can be highly effective against monkeypox, which may help guide how it is used for protecting U.S. personnel in the region.

Developing trusted relationships before crises strike is likewise important. Today this is hindered by BTRP being authorized to work only in specific regions, not globally.

93 Tom Inglesby, "Horsepox and the Need for a New Norm, More Transparency, and Stronger Oversight for Experiments that Pose Pandemic Risks," *PLoS Pathogens* Vol. 14, No. 10, 2018: pp. 1 - 5.

94 Please see Zygmunt F. Dembeck, *USAMRIID's Medical Management of Biological Casualties Handbook, 7th ed.* (Washington, DC: U.S. Government Printing Office Publishing, 2011) and Jeffrey R. Kugelman et al., "Genomic Variability of Monkeypox Virus among Humans, Democratic Republic of the Congo," *Emerging Infectious Diseases* Vol. 20, No. 2, 2014: pp. 232 - 239.

Acting on an urgent threat like a quickly-spreading outbreak requires working within legal and regulatory bounds, and normally requires contracts and agreements to dictate terms of providing donations and assistance. This takes time and knowledgeable personnel, which the United States can only maintain through regular, sustained activities and partnerships over time. For example, a 2020 National Academies report noted that in 2014, as an Ebola crisis was spreading in West Africa, "BTRP was in place well before the declaration by WHO of a Public Health Emergency of International Concern and a vigorous international response could be organized."[95] This preparedness was based on its prior work.

Other unique BTRP authorities make it a powerful tool for the United States in this regard. In particular, its co-mingling authority, by which it can bring in funds from other governments and partners and spend them alongside DoD funds, facilitates rapid responses to emerging threats. The BTRP team should be sure to exercise its co-mingling authority on a regular basis to both ensure its staff can use this ability quickly in crises and benefit from the partnerships it can create.

In the years ahead, BTRP needs leadership---from DoD, other U.S. agencies, and Congress---to expand upon its operational authorities as needed, and exercise them robustly. Providing the program with the ability to operate globally, for example, can be fixed with a straightforward authorization from Congress, as recommended by the 2020 National Academies report.[96]

BTRP activities are still at times hindered by those who view its mission too narrowly and believe it should focus entirely on biological weapons threats. This is a false distinction. COVID-19 has shown the strategic effects and operational issues that a natural outbreak can cause. This perspective reduces DoD's ability to use bio engagement to gain knowledge in key regions and advance strategic partnerships. Such collaboration directly allows DoD to leverage the investments of other governments and philanthropies, and promote capacities that will benefit biodefense and the advancement of defense-relevant technologies. Most importantly, early in an outbreak it is nearly impossible to tell if its cause is natural, deliberate, or the result of an accident.

As such, expanding the range of pathogens under BTRP's focus is an important step. Every new pathogen that is discovered or created that has pandemic potential is a national security concern. As has been seen during the COVID-19 pandemic, pathogens that are deadly and spread quickly can kill millions even with contemporary medical care available.

Its narrower past remit has led to BTRP generally prioritizing work overly focused on especially dangerous pathogens (EDPs) as set by the U.S. Select Agents and Toxins List.[97] However, this can lead to under-valuing or under-utilizing pathogen-agnostic tools that are ideal for detecting and understanding novel pathogens, including those that may be engineered. Such a posture can contribute to missed opportunities to stop outbreaks with the potential to do significant harm to the general public and defense forces. It is also important for BTRP work to touch on pathogens related to those already considered EDPs, given that work surrounding them and access to samples could help confer tacit knowledge and materials that could be used for nefarious purposes. It is crucial for DoD to remain aware of such work as much as possible.

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95 National Academies of Sciences, Engineering, and Medicine, *A Strategic Vision for Biological Threat Reduction: The U.S. Department of Defense and Beyond,* (Washington, DC: The National Academies Press, 2020): p. 31.

96 Ibid, pp. 126-27.

97 U.S. Centers for Disease Control and Prevention and U.S. Department of Agriculture, Federal Select Agent Program, "Select Agents and Toxins List," April 26, 2021.

ATTRACT AND MAINTAIN TALENT

The future success of BTRP in mitigating biological threats will depend on the ability of the Defense Threat Reduction Agency (DTRA) to attract and retain talented people. For 2020, in the Partnership for Public Service's annual survey of best places to work in the federal government, DTRA ranked 213 of 411 agencies.[98] This is actually a significant improvement over its performance in prior years, yet shows the need for continued effort. Countering weapons of mass destruction threats (and biothreats in particular) is a highly attractive mission for talented people, in particular for early-career individuals. DTRA and BTRP program leaders need to continue improving their ability to tap into this interest.

In addition to attracting talented workers to BTRP, the agency will need to keep them. Reducing turnover will be critical. Retention is especially important for threat reduction given how important long-term relationships with international and U.S. interagency partners are to success. Military personnel typically rotate every 2-3 years. Civilian turnover is also affected by the demanding nature of the work itself, among other factors.

These issues can be managed in several ways. For example, pay bands can be altered so that people can remain in the same general job and still have opportunities to grow professionally and obtain good pay increases, as other federal agencies have implemented successfully. This will allow for improvement in the high-payoff, longer term relationship-building described above as critical to understanding and addressing biological threats. An increased budget for BTRP would also allow growth in the program's staff, which would help spread out the high workload and help with retention.

ALIGN INVESTMENTS

Over the coming years, DoD leaders should bring the BTRP budget up to a healthy level and plan to sustain it, for all the reasons this report identifies. Biological threats are rising. Addressing them via cooperative partnerships will help realize broader U.S. security goals. BTRP is a proven asset, and expanding it can be done with a relatively small investment.

As noted above, after several years of budget cuts, the fiscal year 2022 President's Budget Request has included significant further cuts to BTRP: at $124 million, an astonishing 45% cut below the enacted prior year budget.

At minimum, U.S. leaders should raise the BTRP budget to $400 million per year and plan to sustain roughly that level over the next decade. This is slightly above the program's highest funding level in the past decade ($320 million in FY2014). Based on the current President's Budget Request, this would represent under .06% of the 2022 U.S. defense budget---yet pay an incredible return in mitigating and deterring threats. Moreover, the White House has already indicated policy support in this direction.

A common question from Executive Branch and Congressional leaders is how to ensure BTRP activities are not redundant to biological threat reduction programs of other U.S. agencies. As the National Academies recommended in 2020, this should be addressed via a strong White House-led interagency process for coordination and identifying new threats and opportunities.

98 Partnership for Public Service, "2020 Best Places to Work in the Federal Government Rankings - Defense Threat Reduction Agency," 2020.

While currently-rising budgets for other agencies such as the U.S. Agency for International Development are critical for addressing global health security writ large, that will not be sufficient for reducing risks from especially dangerous pathogens or understanding and addressing trends related to deliberate biological threats. Without significant BTRP contributions, the United States will not have the capacity it needs to deter actors' potential interests in biological weapons or strengthen U.S. defense alliances.

CONCLUSION

The stakes are high for appropriately resourcing BTRP in the years ahead. If its investments are not returned to a strong level, relationships with key partners will weaken or sever. The United States will obtain less information about how biological threats are evolving around the world, and the nation will be less effective in deterring actors who may consider the COVID-19 pandemic as proof of the strategic benefits of weaponizing diseases. It is urgent to expand this program as a cornerstone of DoD's efforts to address biological risks.

U.S. DEPARTMENT OF DEFENSE LABORATORIES: UNIQUE, VITAL ASSETS FOR EARLY WARNING AND RESPONSE

U.S. Department of Defense (DoD) laboratories have been a stalwart capability of national security for nearly 100 years. The labs span the U.S. Air Force, Army, and Navy. Biodefense and early warning capabilities could be considered the remit of all of these labs, albeit with a varying focus for each lab. Key research labs, for example, focus on basic science and technology development including for assets to be used as medical or other countermeasures. Examples include the Army Research Lab, the Air Force Research Lab, and the Navy Research Lab.

Other labs are more involved in disease surveillance and early warning. For example:

- The U.S. Air Force School of Aerospace Medicine (USAFSAM) conducts biosurveillance for the Air Force and serves as a reference lab for specific pathogens for other Services.

- The Naval Medical Research Center (NMRC) in Silver Spring, MD, is the headquarters overseeing Naval Medical Research Unit-2 (NAMRU-2) in Southeast Asia, NAMRU-3 in Italy, NAMRU-6 in Peru, and the Naval Health Research Center in San Diego, California.

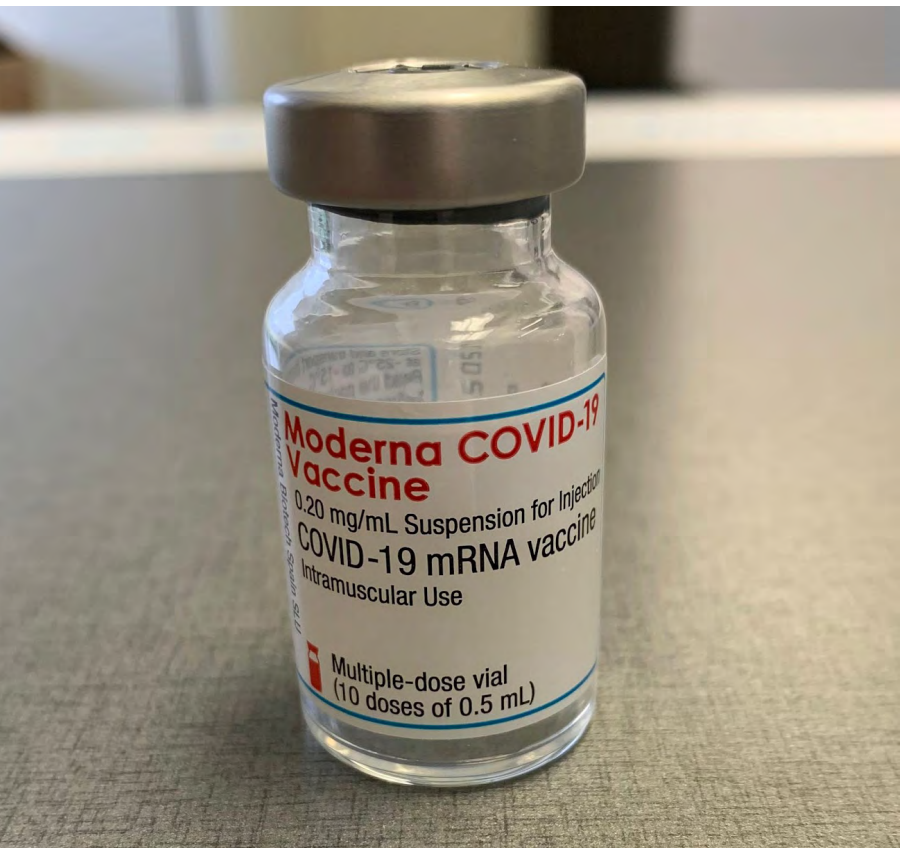
- The Walter Reed Army Institute of Research (WRAIR) in Silver Spring, MD, is the headquarters that oversees labs such as the Armed Forces Research Institute of Medical Sciences (Thailand), U.S. Army Medical Research Unit-Kenya (Kenya), and the U.S. Army Medical Research Directorate-Georgia (Republic of Georgia).

Importantly, DoD's overseas labs conduct only unclassified work, and serve as biodefense assets for the DoD (and the U.S. homeland) as well as the host nations in which they work. In this manner, they exemplify and support military-civilian partnerships, force health protection, and global health security. The labs work in close partnership with the host nation ministries of health, agriculture, and defense, forming an important asset for bilateral and regional cooperation in biodefense, including by facilitating relationships within host government agencies where they are located.

THE DEFENSE ADVANCED RESEARCH PROJECTS AGENCY (DARPA)[99]

COVID-19, the disease caused by the SARS-CoV-2 coronavirus, has clearly demonstrated that the United States is vulnerable to biological threats of pandemic scale. Yet the pandemic has also reinforced the aphorism that necessity is the mother of invention— shining a light on numerous examples of governments making the impossible possible. Consider vaccine development as an exceptional achievement. Historically, it has taken 10–15 years for a vaccine to proceed from research to deployment. The rapid research, development, testing, and production of a COVID-19 vaccine was accomplished in a single year.[100]

An ounce of prevention may be worth several tons of cure, but this value can only be actualized if sufficient investments are made in prevention capacities. The U.S. Defense Advanced Research Projects Agency (DARPA) is such an investor, focusing on funding the development of breakthrough technologies with national security aims.[101] For example, DARPA's Defense Sciences Office (DSO) invested tens of millions of dollars in 2012 in a program called ADEPT:PROTECT, a project that explored using messenger RNA (mRNA) as a platform to deliver "antibody-making instructions," conferring protection against a specific disease.[102] This investment is a salient case where DARPA took the long-range view and developed technology for future use cases that were unspecified, but intuitively anticipated.



Vial of Moderna mRNA vaccine. DARPA made key early investments in mRNA technology, including supporting Moderna. Miquel Tremblay/ Wikimedia

99 Much of the text in this section is drawn directly from Dr. Rohit A. Chitale, Dr. Yong-Bee Lim, and Lillian Parr, "Key U.S. Initiatives for Addressing Biological Threats Part 6: The Defense Advanced Research Projects Agency (DARPA)," Council on Strategic Risks, November 10, 2021.

100 Congressional Research Service, "Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccination Materials," March 1, 2021.

101 DARPA, "About DARPA."

102 For examples, see DARPA, "ADEPT:PROTECT Vignette," 2021; "Preventing Pandemics," January 29, 2021; and "COVID-19," March 19, 2021.

In the midst of COVID-19, it is clear the program paid off. The success of the nearly $40 billion Operation Warp Speed (OWS) which led to the creation, testing, production, and distribution of safe and effective COVID-19 vaccines around the globe has saved countless lives and mitigated worse economic damage. This success would not have been possible without earlier investments in bleeding edge technologies made by DARPA, such as vaccines using nucleic acid vectors.

As government agencies evaluate lessons from the ongoing pandemic, it is important to consider how to best leverage DARPA to address future biological threats. Further, it is important to delve into the organization itself in a bid to optimize its performance against rapidly-evolving biological threats of the future from natural and anthropogenic sources.[103]

This section provides a short background on the Department of Defense's Defense Advanced Research Projects Agency (DARPA). It also provides recommendations for DARPA as the organization grapples with addressing biological threats, both natural or synthetic, within the 21st century's increasingly complex, dynamic threat landscape. Due to its proven potential to impact U.S. national security threats, it is imperative for DARPA to operate at peak efficiency with maximum flexibility to pivot as the biological threat landscape changes, at times abruptly and dramatically.

Further, this section provides key points and considerations to help define DARPA's role in the updated National Biodefense Strategy—a fundamental step in clearly establishing DARPA's position in the biodefense infrastructure. This also helps define a clear lane for DARPA to fully utilize its capacity to address future pandemics and other biological threats for which the exact character is uncertain.

Finally, it is important to note that in this section, we employ COVID-19 as a use case that exemplifies DARPA's mission, operations, and security contributions. However, this is only one example of the panoply of advanced work that DARPA conducts on a daily basis to meet its mission of preventing (and creating) strategic surprise across a wide threat domain.

DARPA: AN OVERVIEW

Created by Congress in 1958, DARPA functions as the central research and development organization of the U.S. Department of Defense.[104] The genesis of its mission dates to the launch of Sputnik in 1957, and a commitment by the United States that from that time forward it would be the initiator and not the victim of strategic technological surprises.

The focus of DARPA is to strive for transformational change. It funds a host of "performers" to achieve these advances, with a constant focus on and collaboration with the nation's military services—DARPA's primary "customers." DARPA strives to take on high-risk, high-reward projects, oftentimes with a magnitude of risk too high for others within and outside the federal government. The term "DARPA hard" has been commonly used to describe efforts it funds.

DARPA has achieved its mission through funding technology development at a variety of organizations within government, academia, and the private sector. In doing so, it has transformed revolutionary concepts into practical capabilities. High-profile outcomes of DARPA-funded research include precision weapons, stealth technology, the Internet, the Global Positioning System, and artificial intelligence (AI) technologies that have been used to make commercially available voice recognition products.

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103 See United States Congress, "The William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021," January 3, 2020; and The White House, *National Biodefense Strategy*, 2018.

104 Annie M. Jacobsen, *The Pentagon's Brain* (Boston, MA: Little, Brown and Company, 2015): p. 5.

The broad category of concepts and capabilities that DARPA works on all share a few characteristics that make DARPA intrinsically a unique organization. First, DARPA funds highly impactful projects—rather than looking to make incremental changes, it seeks to introduce transformative, positive changes in the U.S. strategic landscape. Given the U.S. role in the international community, most will likely have global impact.

Second, DARPA approaches its mission, and the projects it chooses to fund, from a perspective of high risk/high reward. This perspective does not mean that DARPA takes a reckless approach; rather, high risk/high reward in this context refers to the idea that transformation does not happen through piecemeal efforts in existing and well-understood technologies and capabilities. While DARPA attempts to mitigate certain risks by bringing in highly talented experts across multiple disciplines, the organization approaches projects with the understanding that innovation failure rates are exceptionally high in a way that not many other organizations will tolerate. There is an acceptance that failure can and will happen.[105]

Third, this unique ethos of accepting failure makes DARPA an incredibly unique entity across academia, industry, and government. Even other "ARPAs" do not have the funding levels necessary to pursue projects with the level of risk and reward of DARPA.

Finally, DARPA contains both deep internal expertise on technical matters, as well as an impressive network of experts and innovators that span the globe. This enables DARPA to build unique global teams that seek to develop transformative concepts and capabilities. The unique way these multidisciplinary groups can interact and conceptualize problems allows DARPA to visualize and discern vulnerabilities that most other groups may not see. This capability is of particular importance given the complex ways in which emergent and perennial phenomena create strategic changes in the global security arena, including at the intersection of climate change, ecological degradation, and biological threats.[106]

RISKS TO DARPA'S SUCCESS

The agency is not without its challenges, however, in terms of fulfilling its ambitious mission. As input to the development of this section, experts at the Council on Strategic Risks (CSR) interviewed multiple subject matter experts highly familiar with DARPA through their experiences working at or for the agency. Based on these extensive discussions, CSR found multiple potential risks to DARPA's organizational success as it moves forward. Four key areas of concern included:

1) Insufficient biological expertise among leadership within the Director's Office (DIRO) given the potentially catastrophic scale of biological threats;

2) Increased risk aversion within the agency overall;

3) A tendency to regularly move the technical goal posts of DARPA-funded efforts during disruptive times and in disruptive ways; and

4) A lack of stability in prioritizing biological threats.

105 Steve Andriole, "Why Innovation Almost Always Fails," *Forbes*, February 20, 2015.

106 R. Schoonover, C. Cavallo, and I. Caltabiano, "The Security Threat That Binds Us: The Unraveling of Ecological and Natural Security and What the United States Can Do About It." Edited by F. Femia and A. Rezzonico. The Converging Risks Lab, an institute of The Council on Strategic Risks. Washington, DC. February 2021.

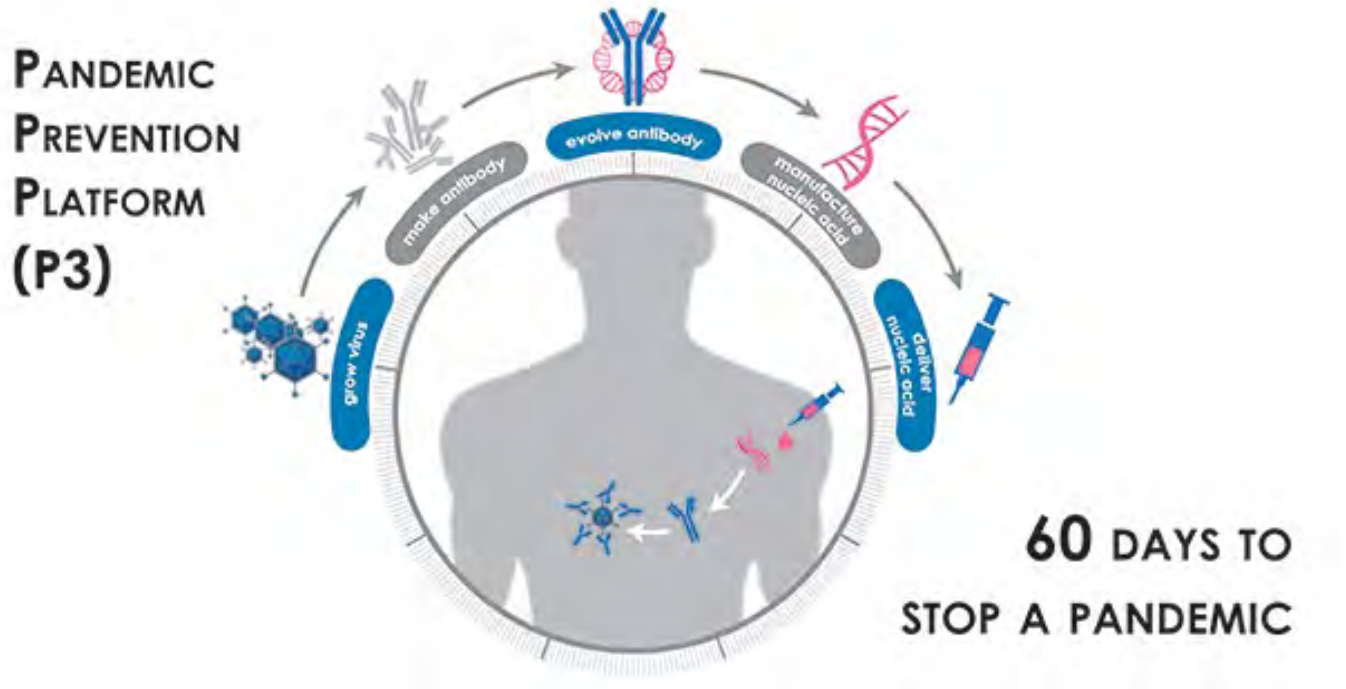
DARPA TODAY

DARPA's office directors and their deputies are responsible for setting their offices' technical direction, hiring program managers, and overseeing program execution. The DARPA Director, a politically appointed position, has discretionary authority over direction and use of DARPA's roughly $3.6 billion annual budget. They are responsible for initial or renewal appointments of program managers, approving new programs, reviewing ongoing programs, and setting agency-wide priorities.

DARPA program timelines, which produce novel technologies, are usually about 3–5 years, which is very temporally aggressive by traditional research standards. This serves to both reinforce the acuity of need for program outcomes, while also placing stringency upon performers to maintain a rapid pace to achieve desired outcomes.

These programs are conceptualized and developed into an approved "program" within DARPA by its Program Managers (PMs). These PMs are subject matter experts in their respective fields, ranging across multiple fields including physics, chemistry, materials science, computer science, molecular biology, epidemiology, genetics, and engineering. These experts and leaders come from academia, industry, and government agencies for limited terms, usually in the range of 2–6 years, based on initial 2-year terms with the potential for 1- or 2-year renewal. The short time spans for programs, and Program Manager tenures, fuel the urgency to achieve success in less time than might be considered reasonable in other agencies.

The DARPA Pandemic Prevention Platform (P3) program aims to support military readiness and global stability through pursuit of novel methods to dramatically accelerate discovery, integration, pre-clinical testing, and manufacturing of medical countermeasures against infectious diseases. DARPA.



Program Managers report directly to DARPA management. DARPA Program Managers are, critically, also supported by technical experts hired as government contractors and known as science, engineering, and technical associates (SETAs), as well as other experts in security, legal and contracting issues, finance, human resources, and communications. These important support staff are tasked with helping program managers succeed in their brief time at DARPA.

DARPA has been exceptionally successful in the past, and continues to operate in new and surprising ways that strengthen U.S. security capabilities, as well as address anticipated global threats. Yet our conversations indicate that several challenges are affecting DARPA's prospects of meeting its potential, including in addressing biological threats. First, many experts indicate a concern that there is too much bureaucracy and attention to minutiae. Second, the rapid turnover of Program Managers introduces harmful churn. Relatedly, there is inadequate respect for and independence of Program Managers. They are often directed in ways that make success more challenging for performers. It is also clear that the inherently short timelines tend to create unneeded volatility, and put program success at risk. And finally, there is a recognized need for greater focus on coordination with the interagency.

Moreover, the global security environment DARPA faces is becoming significantly more complex. A prominent example of this is noting how, despite the availability of safe and effective COVID-19 vaccines, misinformation campaigns have significantly undermined our ability to vaccinate the entire U.S. population. In parallel, phenomena such as gray-zone warfare, borderless disinformation campaigns, and a renewal of strategic competition in the international arena further complicate the biological threat space. On a global level, biological threats are changing and interacting with other systemic phenomena such as climate change and ecological degradation, resulting in significant downstream effects on planetary health, pathogen evolution, spillover, emergence, and disease transmission among humans, animal hosts, and vectors.

Between these dynamics and the internal challenges DARPA faces, the organization is at risk of losing its dominant role in the biological sciences. To meet such complex and interconnected challenges, DARPA must maximize its efficiency and flexibility to prepare for abrupt changes in the threat landscape. DARPA should continue its inclination toward high-risk/high-reward research and development (R&D) efforts, but do so while implementing several recommendations as given in the remainder of this chapter.

RECOMMENDATIONS

It is important for the U.S. government to reignite the transformative spirit of DARPA so that it may continue to drive breakthroughs against biological threats on the scale witnessed in the advancement of mRNA vaccines—and even more groundbreaking work.

IMPROVE ALIGNMENT ACROSS PERSONNEL, RESOURCES, AND PERFORMERS

Culturally, DARPA is meant to be a creative agent of transformation. This requires the confluence of a unique set of organizational and operational traits that enable DARPA to innovate on the bleeding edge. To this end, DARPA can foster these traits on three levels: First, the DARPA Director's Office (DIRO) should provide the overall vision for DARPA— a future-oriented vision that sets a tone and a direction for what DARPA will focus on and prioritize to a) prevent strategic surprise to the United States and b) generate surprise for adversaries by capturing the global strategic

technological high ground. Second, Program Managers, who should be selected for their superlative expertise in a subject area, execute the vision of the DARPA Director's Office at a tactical and/or strategic level. And third, the Technical (Tech) Office Directors, while subject matter experts in their own right, should be selected on the basis of their technical leadership and management skills, with a focus on supporting program managers and programs to execute the vision of the Director's Office within their office.

This section includes recommendations that are general to DARPA but especially important for setting the organization on a strong path for future work in addressing biological threats.

DARPA DIRECTOR'S OFFICE (DIRO)

Recommendation: The Director's Office should implement a vision for DARPA that focuses on high-risk, high-reward research addressing the most pressing threats to national security and Servicemembers.

Given its value as an organization that produces transformational change, the vision of the Director's Office should focus on high-impact projects that set the pace and direction for the technology landscape. It should provide the vision, research, and implementation necessary to lead the pack in terms of the technology landscape. This vision should also be emblematic of the organization's historic high tolerance for risk. DARPA leadership and programs should also embrace a duality of mission: that of support to the military service member, and that of addressing strategic national security needs writ large. That is, it may be critical to design a DARPA program for a national security need instead of focusing primarily on the program's direct benefit to the military service member. Though the "D" in DARPA stands for Defense, DARPA has a very strong brand, and only through continually pushing for high-risk, high-reward, transformative, and rapid outcomes, can DARPA maintain its prominence. It is notable that defending the nation today requires renewed thinking about scope. For example, the fact that climate change is a defense priority evidences the need to widen the aperture of what DARPA can and should address. DARPA projects and programs gain high-level attention, and garner interest from the wider performer community; this then serves to reinforce the DARPA brand. The importance of the sequence of these events, and feedback, should be acknowledged and capitalized upon.

Scoping is also an important component of how the Director's Office will arrive at a transformative, yet feasible, vision given the type of research that DARPA conducts and typical DARPA program timelines (3-5 years). The Director's Office can apply a framework that provides the bounds of what the vision will focus on, consisting of understanding 1) what are the threats to the service member and/or to national security that are of the greatest concern; 2) how can DARPA specifically address these threats; 3) what technologies could be developed or enabled that would contribute to the solution set; and 4) the ways to implement the scoped vision. Particularly in a world that recognizes both the outsized, detrimental impact of an ongoing pandemic, as well as the potentially accelerated rate of emergent biological threats from natural and anthropogenic sources, it is highly recommended that this vision include a significant component that addresses biological threats - a vision that works towards rendering biological weapons obsolete as a mass destruction threat through a bio-focused deterrence by denial strategy.[107]

107 Christine Parthemore and Andy Weber, "A Deterrence by Denial Strategy for Addressing Biological Weapons," *War on the Rocks*, 2021.

TECHNICAL OFFICE LEADERSHIP (I.E., OFFICE DIRECTOR AND DEPUTY DIRECTOR)

Recommendation: Office leadership should commit to supporting the success of Program Managers and distributing funding in a meritocratic manner.

The Office Director and Deputy Director should work toward supporting the vision set by the Director's Office. This begins by recruiting experts in the related field(s) as Program Managers. Office leadership should also work to create synergies among the Program Managers, and ultimately support those same expert managers in achieving their program success (programs that serve the particular DARPA vision, which in turn serves the DARPA mission of preventing strategic surprise). Program Managers come to DARPA for a short period of time in order to "have a baby" in terms of a scientific breakthrough. Presuming that such a scientific breakthrough is something DARPA needs in order to accomplish its vision, DARPA leadership has then only to focus on nurturing that, minimizing interference and roadblocks, and allowing Program Managers and performers to execute on this agreed upon mission and path.

DARPA should further stabilize and empower funding streams for Program Managers by modifying the "wedge" model of funding (allocation) among DARPA Tech Offices—a "zero-sum" type model where a set amount of funding is available on an annual basis to each of the offices.[108] Offices such as Strategic Technologies Office (STO) or Tactical Technologies Office (TTO) often get larger pieces of the pie, while offices such as DSO and BTO get less. These set allocations are determined by the DARPA Director's Office, and each office must work annually within this set amount of funding (i.e., a wedge). This current model, which creates competition for a limited amount of resources across multiple projects, should be modified into a model that is much more meritocracy-based: one in which the best ideas with the greatest impact (from the fresh talent and perspectives constantly flowing into DARPA) get incentivized via greater funding. This is a dynamic that is particularly important to cultivate as there is substantial and increasing competition for talent in the innovation and technology sectors— across government, academia, and the private sector. Over time, if not effectively addressed, this could result in significant talent loss for DARPA.

PROGRAM MANAGERS (PMs)

Recommendation: DARPA should take a bottom-up approach, allowing Program Managers independence in designing and implementing projects.

A well-known and long-serving former DARPA Director had the tendency to directly supervise Program Managers.[109] This contributed to discussions on whether the agency should be bottom-up, or espouse the typical top-down leadership approach. A subsequent DARPA Director later instituted the position of "Office Director," adding a management layer in between the Director's Office and the Program Managers. As recently as one year ago, a previous DARPA Director had said that "PMs are the kings and queens of DARPA," emphasizing the need for more of a bottom-up approach, with a strong focus on the Program Managers, and less so on any layers in between the Director's Office and the Program Manager. DARPA directors have had different managerial styles and instituted different reporting chains, leading to confusion regarding the directionality of reporting.

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108 Erica Fuchs, "Cloning DARPA Successfully." *Issues in Science and Technology* Vol. 26, No. 1 (2009): pp. 65–70.

109 Patrick Windham and Richard Van Atta, "Introduction: DARPA—The Innovation Icon," in *The DARPA Model for Transformative Technologies: Perspectives on the U.S. Defense Advanced Research Projects Agency,* ed. William B. Bonvillian, Richard Van Atta, and Patrick Windham (Cambridge, UK: Open Book Publishers, 2019): p. 7.

Our recommendation is that the right choice is a bottom-up approach. Program Managers and performers (including sub-performers) are the drivers when it comes to project ideation, conceptualization, design, and implementation. This usually means operating in a fast-paced environment where performers must meet exceptionally difficult goals with very little slack built into the project timeline. Therefore, it should be acknowledged that the Program Managers and performers are those that have the deepest knowledge and the best understanding of ongoing projects in their portfolio, usually in their own fields of expertise.

IMPROVE FUNDING MECHANISMS AND SOURCES

Recommendation: Program Managers should be given a discretionary budget to fund promising research proposed through office-wide broad agency announcements.

Each Technical Office at DARPA has available, via the DARPA website, a standing, broadly scoped office-wide broad agency announcement (BAA) to which anyone can submit (propose) their "innovative" ideas. This is potentially an excellent method for capturing and developing truly innovative ideas from potential performers that might not otherwise be able to respond to pre-existing and usually announced opportunities. Nonetheless, the current process of the office-wide broad agency announcement needs optimization. Funding for any efforts selected under the office-wide announcements typically comes from program funds within the selecting Program Manager's portfolio (of funds under their control). Therefore, in order to fund a separate effort, a Program Manager is forced to divert resources from their existing programs to take a risk on any appealing technologies that come through this mechanism.

A solution to this is the provision of a discretionary seedling budget to Program Managers that is outside of program budgets. Thus, without having to "rob Peter to pay Paul," Program Managers could use their discretionary "seedling" budget to explore and de-risk technologies proposed through the office-wide broad agency announcement, without having to take funds from an existing program's budget. Taking funds from an existing program contributes to undoing the substantial efforts put into creating that well-considered budget, effectively wasting time and resources.

Further, to enhance this process, along with a discretionary seedling budget for Program Managers, any proposals being reviewed through the office-wide announcement submission process should have higher requirements for consideration, such as the proposer having completed a moderately detailed Heilmeier Question (HQ) document.[110] Prescreening and greater requirements will reduce the reviewing burden on Program Managers for these submissions, and the greater availability of funding, together, will increase the relative rate of selection of these office-wide announcement submissions.

Finally, increased communication or marketing of this process should serve to encourage submissions and increase their overall quality. This is particularly important for the life sciences, where the emergence of the biotechnology revolution and the promise of the bioeconomy are developing a thriving ecosystem of new technologies and platforms. Given the start-up culture of biotech at this stage, applying DARPA's high-risk/high-reward strategy to funding seedling efforts could increase the throughput of potential promising technologies being evaluated - which would serve to cultivate and attract the best and the most innovative start-up companies for DARPA funding opportunities.

110 Jinendra Ranka, "DARPA: Enabling Technological Innovation," in *The DARPA Model for Transformative Technologies: Perspectives on the U.S. Defense Advanced Research Projects Agency*, ed. William B. Bonvillian, Richard Van Atta, and Patrick Windham (Cambridge, UK: Open Book Publishers, 2019): p. 310.

REACH FARTHER AND WIDER FOR DARPA PERFORMERS

Recommendation: DARPA should ensure that it seeks performers who will produce the highest quality work, including those from outside of the United States.

Researchers funded under DARPA projects are those who do the innovative work of and for DARPA, under the watchful eye of the Program Managers. These researchers are known as "performers." The choice of these performers is vital, and a great deal of time is spent by DARPA staff on selecting, vetting and then managing these performers. Therefore, it is essential to ensure that the right performers are selected for a program or a seedling (the latter being a small, short, exploratory effort). However, there has been a tendency of some performers to try and "game" the system by knowing how to prepare slides that will appeal to DARPA, or use the right verbiage to sell their technological prowess to DARPA. This has led to the same performer often receiving multiple awards from DARPA, and not necessarily DARPA choosing the best performer for the effort.

A key recommendation is that DARPA must enhance diversity in terms of the participants and their geographies. This wider look, especially for non-U.S. performers, can introduce novel technologies stemming from geographies usually not considered by DARPA, and also lead to cost savings—both of strong interest to DARPA and the nation. This can build on the long tradition of the Department of Defense collaborating with allies and other international partners in addressing biological threats, which will be important to both developing the best technologies in this regard and deterring biological weapons activities.

FIND BALANCE IN PACING

Recommendation: Extend terms of DARPA Office Directors and Program Managers to improve stability while still maintaining flexibility and agility.

DARPA is an organization that moves rapidly, with exceptionally short timelines. Program Managers and office leadership terms are also brief. Though this is by design and intended to seek results quickly, it also requires high maintenance and can introduce harmful churn. In order to find balance between the pursuit of impactful results and potentially-harmful attrition, some key issues should be addressed.

The short timelines of programs and brief tenures of staff are baked into DARPA culture and serve to maintain a brisk pace of technological development. Nevertheless, Program Managers almost never see the completion of programs they start, and there is always the potential for a new Program Manager or new office leadership to terminate existing programs or seedlings, also leading to wasted taxpayer dollars. Measures should be taken to avoid disruption of these programs and vision as Program Managers and leadership change. While one Director's or Program Manager's priorities might differ from the next, presumably there is still value in both, and especially in the short time spans under consideration. It would be wasteful to abort successful programs simply because new management has less interest in them.

The DARPA Biological Technologies Office (BTO) has had 4 Office Directors in 7 years. The DARPA Director's Office has had a little less turnover, though as the DARPA Director is politically appointed, this turnover is harder to modify. What can and should be addressed are the more regular changes of the Office Director, Office Deputy, and, most importantly, the Program Managers who are hired and then directed to manage the technology developments that define DARPA's success—and national security outcomes.

Jennifer Doudna at TEDGlobal London. Jennifer Doudna won the Nobel Prize for Chemistry in 2021 for her work on the gene editing technology CRISPR. The biotechnology company Mammoth Biosciences, which she cofounded, is working with DARPA to develop CRISPR-based pathogen detection technologies. James Duncan Davidson/TED

Additionally, the rapid turnover of Program Managers can lead to a confusing and inconsistent environment that is detrimental to research, which in turn makes researchers less likely to apply for DARPA funding. This trend has been seen over recent years, with indications that performers might prefer to seek funding from other U.S. government agencies that have similar performance standards because of the reduced managerial and administrative demands. Though the DARPA brand is strong, recent conversations with subject matter experts in the field indicate a reduced desire to seek DARPA funding because of it being deemed onerous to deal with the agency.[111]

DARPA Office Director and Program Manager terms should be lengthened in order to foster stability. The current term length of 2 years to start, with 1- or 2-year extensions, is short by design; DARPA staff regularly speak about their "badge date" as a reference to the date when the individual's DARPA term is due to end. The expectation is that a 1- or 2-year term will be extended, but there is no guarantee and this is mainly reliant on the decision of the Office Director, despite the final decision by and signatory being the DARPA Director. These short terms introduce instability that should be mitigated by lengthening the term. With longer terms, such as 4 to 5 years, Program Managers can focus on developing and then managing programs for a greater amount of time, which allows for continuity and stability within Program Manager tenures and careers. All U.S. employees are "at-will" and can still leave at any time. Yet, increasing the term length would allow a Program Manager who wishes to stay for the duration to do so, and thus maintain some stability among their programs and vision. This stability is vital given how projects that have yielded

111 This is based on conversations with nearly two dozen subject matter experts who were consulted by the authors to help define and explore these recommendations on a non-attribution basis.

such significant results for the United States, such as early mRNA technology research and development, are not done within the span of 3 - 5 years: even the mRNA technologies that formed the basis for COVID-19 vaccines took over a decade to mature. Program Managers come to DARPA to support the nation and make a transformational change in the world through developing novel technology; current 2-year terms do not support this outcome.[112]

REVAMP DARPA PROCESSES FOR DEVELOPING BIOLOGICAL TECHNOLOGIES

Recommendation: DARPA should revamp the Biological Technologies Office to better suit conducting biological research and should increase the number of staff with biological expertise in leadership roles.

The Biological Technologies Office (BTO) was spun out of the Defense Sciences Office (DSO) and created in 2014. Per the DARPA BTO website, BTO "develops capabilities that embrace the unique properties of biology—adaptation, replication, complexity— and applies those features to revolutionize how the United States defends the homeland and prepares and protects its Soldiers, Sailors, Airmen, and Marines" and "helps the Department of Defense expand technology-driven capabilities to detect novel threats and protect U.S. force readiness, deploy physiological interventions to maintain operational advantage, support warfighter performance, and focus on operational biotechnology for mission success."[113]

The DARPA BTO was added as a sixth technical office in 2014 and has largely followed the same processes of the other five technical offices. However, it has become increasingly clear that there are some key differences from the other offices that should be addressed moving forward. Such differences surround the content covered by the BTO, specifically that of studying and using biology to develop technologies. Biological technology development is unlike that of abiotic systems; with biological technology development, "speed of development" and "safety" do not inherently go together. DARPA must acknowledge this as it moves forward. Also, with biological technology there is a substantial commercial market, making harder the choice of what to focus on for DARPA as it works to accomplish its mission of preventing technological surprise.

Branding is something that is incredibly important for any organization that wishes to build a consumer base and let consumers know the products or services the brand provides.[114] Currently, the name and brand of the DARPA BTO may inadvertently be constricting the scope of the office; the BTO, and DARPA writ-large, are today considered only a "tool developer." To address this issue, DARPA should consider changing the name and scope of the Biological Technologies Office to the Biological Sciences Office. This would clarify how DARPA's role is not restricted to only developing capabilities and tools—in reality, DARPA more broadly functions as a biological systems analyst and influencer. Technical areas of interest to DARPA garner attention from other U.S. agencies and other funders (e.g., foundations), and ultimately catalyze overall investment in a specific area. Potentially more than other fields, basic science is needed in biology to develop technologies, and the focus should also be on early technology levels for DARPA. It should be acknowledged that technology development is but one way in which biological systems can be influenced.

Further, given recent examples and acknowledged importance of addressing biological threats, it is necessary to have sufficient DARPA staff that can represent a broad range of biological expertise from molecular to ecological scales,

112 Paul Sonne, "How a Secretive Pentagon Agency Seeded the Ground for a Rapid Coronavirus Cure," *The Washington Post*, 2020.

113 DARPA, "Biological Technologies Office."

114 Kristopher Jones and Forbes Agency Council, "The Importance of Branding in Business," *Forbes*, March 24, 2021.

with an emphasis placed on attracting individuals with multi-scale knowledge application and the demonstrated ability to assess R&D feasibility across biological scales. These staff members should also be distributed across all levels of the DARPA organization, ranging from Program Managers to the DARPA Director's Office level— a necessity to ensure that expertise is readily available in this area to both incorporate knowledge of biological issues in-house, as well as maintaining strong advocates across the organization for giving biological threats the attention they deserve.

Finally, there is a strong need to constructively address the conflict between DARPA's tight program timelines and the timeframes inherent in biological processes and regulations involving biological research. There are inherent tensions between DARPA's accelerated timeframe and the limitations that are imposed by elements in any life sciences studies, ranging from the molecular and organismal to the ecological scale. Just to name a few examples: sequencing can be inaccurate, transformations may take significant amounts of time to generate the right colony, evolution and characterization of viral quasispecies require time and repetition, and animal models are limited by the number of animals that match the stringent life sciences research requirements. Of particular concern is how DARPA timelines may push performers to work in lower biosafety levels than what may be prudent, based on the potential biological threats present in uncharacterized samples.

To address these issues, DARPA should conduct a review of time-limiting factors, and find ways to address them through novel capabilities or processes such as running portions of a study in parallel. DARPA should also look to organizations that have past experience in issues like this, such as the National Science Foundation and other federal science funders, for lessons learned. Finally, DARPA should enable greater flexibility in milestones for biological research, permitting researchers to pace themselves according to basic safety, animal welfare, and biological process requirements.

IMPROVE TRANSITIONS FROM DARPA TECHNOLOGIES

Recommendation: DARPA should place more emphasis on identifying transition partners and engaging with them through all stages of program development.

The "Valley of Death" is a well-known concept in technology development that represents the phase between early-stage development and later stage development, moving toward commercialization.[115] It is critical at the outset to find appropriate transition partners to facilitate R&D into the commercial space. Oftentimes, DARPA seeks a partner that is a military Service (Army, Navy, Air Force, etc.), but it is also the case that sometimes the military is not the appropriate transition partner.

Transitioning has always received short shrift at DARPA, in part because of the rapid personnel turnover. Since DARPA programs are usually 3–5 years in length, and Program Manager tenures are 2–6 years, it is rare that a Program Manager will conclude or transition a program that they have started. Because of the substantial effort involved in developing a program and getting it approved, transition can often be overlooked as a problem for the future. However, with the aforementioned regulatory concerns, transition is of particular importance for biological technologies, and novel strategies such as those mentioned above should be taken to facilitate and ensure successful transition of DARPA-funded research and development.

The fairly recent addition of the DARPA Embedded Entrepreneur Initiative (EEI) was a strong step toward supporting transition efforts, designed to accelerate innovations to products and help DARPA research teams.[116] The initiative provides

115 Defense Advanced Research Projects Agency, "Innovation at DARPA," July 2016.

116 Defense Advanced Research Projects Agency, "The Embedded Entrepreneurship Initiative."

funding and mentoring to DARPA performers, and connections to investors and corporate partners. It focuses on the performers and provides entrepreneurial skills, an understanding of private sector market dynamics, and business expertise.

However, there remains the need for addressing transition earlier in a program timeline. Therefore, we recommend that the U.S. Department of Commerce and U.S. Department of Health and Human Services be better engaged from the start. They could be strong partners as DARPA Program Managers develop programs, and through all stages of program development. A group that can "pick up" the technology development (e.g., running clinical trials in humans or animals, moving forward with regulatory processes) at the stage where DARPA is finished is very important and should be identified as early as possible.

In addition, adding a liaison officer (LNO) for identified or likely transition partners would be a key step in optimizing the technology transition process. The liaison officer would provide knowledge of, and reachback capability into, their home organization, and links with DARPA. Liaison officers at DARPA from other agencies could be consulted early on in DARPA program development, and help shepherd programs after the DARPA funded effort to transition efforts. Examples of some key partners could be the Defense Threat Reduction Agency (DTRA), the Joint Program Executive Office for Chemical, Biological, Radiological, and Nuclear Defense (JPEO-CBRND), and the HHS Biomedical Advanced Research Development Authority (BARDA). Similarly, liaison officers from key regulatory agencies such as the Environmental Protection Agency (EPA), Food and Drug Administration (FDA) and U.S. Department of Agriculture (USDA), jointly funded, would be very valuable to help with transitioning DARPA-funded technologies.

REGULATORY ISSUES & DARPA

Biological science is understandably much more heavily regulated than other fields. To conduct animal or human studies, important approval processes consume a minimum of four months of program time before work can even begin. Delays caused by this time requirement could be mitigated by having a standard practice of approving "No Cost Extensions" (NCEs) that adjust for the review time period of the Institutional Review Board (IRB), Animal Care and Use and Review Office (ACURO), and the Human Research Protection Office (HRPO). Usually following a DARPA program - after preliminary research has been conducted - any product intended for human or animal use requires regulatory approval from the FDA or USDA. This is an approval process that is beyond even DARPA's large budget and accelerated timelines. However, any delays with respect to these timelines could be mitigated by changing the expectation of a product at the conclusion of a BTO program, via the early consultation of a regulatory liaison officer (LNO), and facilitating appropriate partnering with, or transition to, an entity that has both the will and resources to complete the regulatory process. This entity might itself be a separate agency, or else DARPA could work closely with the regulatory LNO.

CONCLUSION

DARPA is approaching an inflection point with respect to biological sciences and technologies. The global epidemiology of the COVID-19 pandemic itself, as well as the continued uncertainty with respect to the origins of the COVID-19 virus, are stark reminders of the complexity of today's world and especially that of the biological sciences. It is hoped that through reflecting on recommendations put forth in this document, DARPA will continue to lead the pack in making transformational changes that address biological threats—be it via disease prevention, detection, or treatment. American lives depend on DARPA's success.

GETTING INTELLIGENCE TO THE RIGHT PEOPLE

Intelligence officials rely heavily on the demand signals they receive from national security leaders to inform their priorities and share intelligence updates appropriately. Put simply, if key leaders show little interest in catastrophic biological threats and trends, it is unlikely that the intelligence community will prioritize it.

In practice, there are multiple steps that people in key positions should take regularly in order to create a greater demand-pull for intelligence reporting and analysis regarding biological risks (of course, maintaining the need-to-know basis of receiving such intelligence). For the Department of Defense, the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs can play an important role. For example, people serving in this position should:

- Request updates from their intelligence briefers monthly, quarterly, or as warranted on key countries and issues of concern for biological threats. This may include such countries' activities that defy broadly-accepted norms and treaties, such as chemical weapons concerns, as well as gain-of-function and other high-risk research.

- If they do not already receive regular updates, help set up and join classified briefings on biological weapons threats to the Secretary and Deputy Secretary of Defense, Director for Cost Assessment and Program Evaluation, Under Secretaries of Acquisition & Sustainment and Research & Engineering, and the DARPA Director. They should also set conversations on the subject with Joint Staff leads and Combatant Commanders (when possible via trips to command headquarters).

- Hold regular discussions with regionally-focused counterparts, for example assistant secretaries focused on the Indo-Pacific and European regions.

- Encourage the Executive Office of the President focal point for addressing biological threats to carry out similar practices for the National Security Advisor and other key White House leaders.

Equally important, these officials can accompany intelligence briefings with their own updates on the solutions that the Department of Defense and other agencies are pursuing. This can help foster and strengthen relationships between intelligence officials and interagency officials in two ways. First, it provides opportunities for the intelligence community and interagency to have conversations and engage in an iterative process together. This process is important given that changes in circumstances and requirements can have a significant impact on intelligence community data collection and analysis. Second, it enables a broader range of actors to better understand the programmatic approaches and budgets the nation is pursuing and why those investments are so valuable.

Exterior sign for the U.S. Army Institute for Infectious Disease (USAMRIID). Department of Defense.

USAMRIID

The United States Army Medical Research Institute of Infectious Disease (USAMRIID) has historically been seen as the world's premier biodefense facility. Over decades, USAMRIID has built expertise and capabilities to protect U.S. military personnel from weaponized pathogens.

USAMRIID develops medical countermeasures, which entails research to better understand the world's most dangerous pathogens and development, testing, and evaluation of treatments and vaccines against those same pathogens. It is also home to the only maximum containment laboratory (BSL-4) in the Department of Defense (DoD). As an example of its recent work, USAMRIID personnel helped develop one of the first treatments to significantly reduce the fatality rate of Ebola, both a naturally arising virus and one that is concerning as a potential biological weapon.[117]

USAMRIID is an irreplaceable national asset for countering biological threats. Yet despite its storied history and incredible capabilities, USAMRIID now stands at an inflection point. In recent years it made headlines more for issues of deteriorating infrastructure and lab safety (which have been addressed) than for its contributions to the

117 "USAMRIID Receives Tech Transfer Award for ZMapp Contributions," *Global Biodefense,* 2016.

nation.[118] Though USAMRIID has a new $3 billion, cutting-edge headquarters and laboratory, there is a serious risk of it being underused. The institution has lost experts to other U.S. agencies, the private sector, and academia, with continuing indications of frustrations among staff that they are underused and insufficiently connected to scientific progress and innovation outside of defense circles.

The worst biological event of the century so far—the COVID-19 pandemic—showcases the need for the United States to move quickly to determine a strong future for USAMRIID. This section is based on conversations by the Council on Strategic Risks (CSR) team with former USAMRIID commanders and leading experts, and others in the DoD biodefense enterprise. It recommends the following:

1. **U.S. policymakers should refocus USAMRIID's mission:** USAMRIID's explicit mission should be the development of medical countermeasures against biological weapons and highly pathogenic emerging infectious diseases, with increasing focus on platform approaches.

2. **U.S. policymakers should consider creative options for USAMRIID's structure:** USAMRIID has become more of a biodefense support facility than a premier source of solutions to the most significant biological threats the United States faces. To fully take advantage of USAMRIID's new laboratory and headquarters and its world-class talent, USAMRIID should be granted more independence. Options include converting it to a DoD Federally Funded Research and Development Center (FFRDC), enhancing the budget of the Chemical and Biological Defense Program (CBDP) to better utilize and support USAMRIID scientific excellence, or a combination of both. U.S. leaders should also consider merging it with the Walter Reed Army Institute of Research and splitting organizational roles based on biocontainment requirements.

3. **Congress should require a Government Accountability Office (GAO) report on talent and organizational challenges:** The institute is losing expertise and knowledge that has taken decades to build. Congress must be kept abreast of the erosion of USAMRIID talent and use GAO recommendations to craft legislation, track progress, and explore organizational changes to reverse this trend.

REFOCUS USAMRIID'S MISSION

In months, the SARS-CoV-2 virus spread from a local outbreak to a global pandemic. Two years later, the virus is continuing to rampage across the world and evolve. It will likely become an enduring threat to public health broadly and U.S. military forces specifically.[119] Experts attribute the virus's death toll and global reach to its exploitation of vulnerabilities in pandemic prevention systems: because SARS-CoV-2 was novel, healthcare providers had no targeted medical countermeasures to treat its infections. In addition, today's early warning systems have difficulty spotting pathogens that spread asymptomatically---one of the primary reasons the virus is so difficult to track and contain.[120]

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118 Please see Denise Grady, "Deadly Germ Research is Shut Down at Army Lab Over Safety Concerns," *The New York Times*, 2019; and Patricia Kime, "CDC Lifts Shutdown Order on Army Biolabs at Fort Detrick," *Military.com*, 2020.

119 Nicky Phillips, "The Coronavirus Is Here to Stay — Here's What That Means," *Nature News Feature*, 2021.

120 Seyed M. Moghadas, Meagan C. Fitzpatrick, Pratha Sah, Abhishek Pandey, Affan Shoukat, Burton H. Singer, and Alison P. Galvani, "The Implications of Silent Transmission for the Control of Covid-19 Outbreaks," *Proceedings of the National Academy of Sciences* Vol. 117, No. 30, 2020: pp. 17513-17515.

Defense Secretary Dr. Mark T. Esper tours the U.S Army Medical Research Institute of Infectious Diseases (USAMRID) with Army Brig. Gen. Mike Talley, commanding general of U.S. Army Medical Research Development Command (USARMDC) during his visit to Fort Detrick, Md., March 17, 2020. Army Staff Sergeant Nicole Mejia/Department of Defense

SARS-CoV-2's success relied on evolutionary mutations that increased its spread. U.S. adversaries considering development of biological weapons could purposefully select or engineer pathogens that exploit these and other vulnerabilities.

The United States should position USAMRIID to address these types of challenges and fulfill its potential as one of the nation's top assets for addressing biological threats. A smart path forward is to 1) expand its mission to perform a wider range of scientific and technological work and 2) ensure it is used for pandemic-potential biological threats of natural and accidental origin, in addition to potential biological weapons.

The 2006 Quadrennial Defense Review, the guiding high-level strategic document for the DoD at that time and the precursor to the U.S. government's National Defense Strategy, directed the DoD to invest $1.5 billion over the next five years to counter a diverse portfolio of bioterror threats.[121] This program was called the Transformational Medical Technology Initiative (TMTI), and the goal was to research platform approaches to medical countermeasure development and to discover medical countermeasures effective against multiple pathogens. The CBDP conducted much of the initiative's activity at USAMRIID.

121 U.S. Department of Defense, Chemical and Biological Defense Program, *Transformational Medical Technologies Initiative (TMTI) OUSD (AT&L) FY 2007*, (Washington, DC: U.S. Government Publishing Office, 2007).

Subsequently, the emphasis on USAMRIID's testing and evaluation mission significantly expanded.[122] USAMRIID has unique capacities to conduct efficacy trials in accordance with the Food and Drug Administration's Animal Rule, which is used for the testing and evaluation of medical countermeasures for pathogens that are highly pathogenic. For the last several years, the majority of CBDP funding for USAMRIID has been for such testing and evaluation work, in addition to investments for maintaining and expanding existing USAMRIID facilities and capabilities.[123]

This also stems from CBDP's narrow mission. That mission should be expanded to include deterrence and pandemic prevention, as described above, and not just to "anticipate future threats and deliver capabilities that enable the Joint Force to fight and win in CB-contested environments" as it stands today.[124] With a broader mission and span of activities, USAMRIID can once again become a central component of U.S. deterrence.

It is urgent now for policymakers to ensure USAMRIID's capacities are more fully utilized going forward. USAMRIID should focus on both basic and applied research and development, especially advanced platform approaches for medical countermeasure development that can be used to rapidly create treatments or vaccines for any dangerous pathogen. The pharmaceutical companies Pfizer, BioNTech, and Moderna showed the world the benefits of a platform approach in their rapid development of highly effective mRNA vaccines against COVID-19.

Traditionally, USAMRIID developed medical countermeasures in response to intelligence community reporting on other nations' biological weapons programs.[125] Such work should be increased, with USAMRIID emphasizing versatile platform approaches that will make it easier to have consistent success in rapidly creating medical countermeasures against biological weapons threats, including engineered ones.[126]

At the same time, USAMRIID should expand its mission to explicitly include emerging infectious disease threats. In October 2019, the Johns Hopkins Center for Health Security hosted an exercise to simulate the public health response to an outbreak of a novel pathogen.[127] For the exercise, the organizers posited an outbreak of a novel coronavirus that participants found difficult to contain, leading to sixty-five million deaths.[128] There is evidence that in that month an actual novel coronavirus—SARS-CoV-2—may have already been spreading.[129]

Incongruously, because of existing policy, DoD separates biodefense organizations into those responsible for reducing deliberate biological threats and those that work on naturally arising ones. This artificial divide causes numerous problems and inefficiencies. For example, during the COVID-19 pandemic, based on conversations between this report's authors and various Congressional staffers and DoD officials, it appears that DoD prohibited spending Defense-wide CBDP program funds to aid in the development of medical countermeasures against COVID-19. Especially as the origin of a pathogen may not be immediately apparent, this distinction is often arbitrary and detrimental to effective responses to potentially-catastrophic biological threats.

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122 Ibid.

123 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission," (Washington, DC: U.S. Government Publishing Office, 2021).

124 Office of the Assistant Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs, Chemical and Biological Defense, CBD Vision, accessed November 2021.

125 U.S. Government Accountability Office, *Biodefense: Federal Efforts to Develop Biological Threat Awareness* (Washington, DC: U.S. Government Publishing Office, 2017).

126 Jason Matheny, Michael Mair, and Bradley Smith, "Cost/Success Projections for U.S. Biodefense Countermeasure Development," *Nature Biotechnology* Vol. 26, No. 9, 2008: pp. 981-983.

127 Katie Pearce, "Pandemic Simulation Exercise Spotlights Massive Preparedness Gap," *Johns Hopkins Center for Health Security,* 2019.

128 "Event 201 Scenario," *Johns Hopkins Center for Health Security*, 2019.

129 Jonathan Pekar, Michael Worobey, Niema Moshiri, Konrad Scheffler, and Joel O. Wertheim, "Timing the SARS-CoV-2 Index Case in Hubei Province," *Science* Vol. 372, No. 6540, 2021: pp. 412-417.

The U.S Army Medical Research Institute Has Years of Ebola Drug Expertise. Dr. John M. Dye Jr., Viral Immunology branch chief, working on ZMapp, a treatment for Ebola patients. USAMRIID.

Artificial delineations between deliberate and natural biological threats contribute to USAMRIID being underused. Rather, the designation should be based on the assessed threat to national security. This would take into account all factors related to deliberate biological threats, as well as biological factors that contribute to the potential scale of naturally-arising threats such as infectivity, pathogenicity, and availability of countermeasures. This is roughly approximated by biosafety containment level. USAMRIID is home to one of the largest BSL-4 high-containment laboratory facilities in the world and should conduct research on the most dangerous pathogens of all origins.[130]

CONSIDER CREATIVE OPTIONS FOR USAMRIID'S STRUCTURE

Early in the COVID-19 pandemic, then-Secretary of Defense Mark Esper visited USAMRIID, telling reporters, "If anybody knows how to do it [take on the coronavirus], they know how to do it."[131] But USAMRIID was not empowered to undertake work fighting the virus until agreements were made with other U.S. government entities. USAMRIID's dependence on other organizations for direction and funding for explicit lines of effort, and an inability to initiate work without such funding, is a key underlying problem.

USAMRIID is an unusual organization. Based on its current model, it has more in common with a government contractor than a DoD unit. In a reorganization that occurred after the first Gulf War, USAMRIID lost direct research funding and became reliant on other organizations, especially the Defense Threat Reduction Agency, to fund

130 "WSP USA Provides Expertise for World's Largest High-Containment Research Lab," *WSP*, 2019.

131 John M. Donnelly, "Army Lab Fights Coronavirus and Its Own Demons," *Roll Call*, 2020.

and direct its activity. USAMRIID remains the home of the nation's top biodefense talent and facilities, yet it must compete for funding from other organizations. In the case of the COVID-19 pandemic, because of the aforementioned policy decision prohibiting the use of CBDP funding, USAMRIID was unable to immediately mobilize its significant resources towards pandemic response and had to await agreements with government customers.[132]

Policymakers should consider revamping USAMRIID as a DoD FFRDC. For such a transition, the Office of the Under Secretary of Defense for Acquisition and Sustainment would be a natural FFRDC sponsor since it is responsible for the majority of DoD research and development to reduce biological threats. USAMRIID would have more independence to pursue the research its top scientists view as valuable, and would be less subject to the U.S. Army's traditional hierarchy.[133] Just as important, as an FFRDC, USAMRIID would have its own funding.

U.S. Army Pfc. Kaiya Capuchino (left), United States Army Medical Research Institute of Infectious Diseases (USAMRIID) combat medic, helps a student don personal protective equipment during hazardous material training Oct. 30, 2014, at Tripler Army Medical Center, Hawaii. Members of the USAMRIID conducted the class to help ensure service members and civilians are better prepared to react to and defend themselves against infectious diseases at TAMC. Staff Sgt. Christopher Hubenthal/U.S. Air Force

132 *Future of USAMRIID* (discussion held under the Chatham House Rule), Council on Strategic Risks, July 27, 2021. For more organizational dynamics see: Joseph Kirschbaum, Mark A. Pross, Richard Burkard, Russ Burnett, Jennifer Cheung, Rajiv D Cruz, Karen Doran, Edward George, Mary C. Hult, and Mae Jones, *Chemical and Biological Defense: Designated Entity Needed to Identify, Align, and Manage DOD's Infrastructure*, U.S. Government Accountability Office, (Washington, DC: U.S. Government Publishing Office, 2015).

133 For more information on FFRDCs, please see: U.S. Congress - Congressional Research Service, *Federally Funded Research and Development Centers (FFRDCs): Background and Issues for Congress*, 2020.

If USAMRIID is transformed into an FFRDC, the CBDP will still require testing and evaluation facilities for medical countermeasures against the world's deadliest diseases. This critical work should continue to be conducted at USAMRIID's facilities. Yet in this type of reorganization, USAMRIID can be structured to engage in work beyond testing and evaluation (e.g., more early-stage research) and for a broader range of partners. An initial step toward this reorganization would be for DoD or Congress to commission a study to further detail transitioning USAMRIID to becoming an FFRDC and also explore other models that grant USAMRIID more control over its research and development agenda.

Changing the legal structure of USAMRIID is one option. Another is a simple, shorter-term fix: direct the CBDP to fund more work at USAMRIID and increase the CBDP budget to make this possible.

CBDP provides the majority of USAMRIID's funding and has seen large reductions in its own spending power over the last decade. In comparison to the 2005-2010 period, CBDP spending power (budget adjusted for inflation) has been reduced by almost a third, creating follow-on effects and funding uncertainty at USAMRIID.[134] Former USAMRIID leaders have lamented the difficulties of planning when CBDP funding is decreasing and unpredictable. As a general purpose intervention, and one that can pre-date broader organizational changes, increasing annual funding for the CBDP would help ensure that USAMRIID receives more consistent resources.

CBDP can use additional funding to start the process of refocusing USAMRIID's mission. CBDP should increase investments in programs to develop standardized platform approaches to medical countermeasure development against the deadliest diseases that require maximum containment facilities. Examples of ongoing programs that should receive increases include new platform medical countermeasures based on nanosponges, which mimic human cells to attract and neutralize viruses in a patient. This work is being conducted within a project called Techbase Medical Defense - Applied Research and in the Bacterial/Viral/Toxins/Broad Spectrum Prophylaxis program.[135]

Another example is standardized processes for developing medical countermeasures that build on the success of the Pfizer and Moderna vaccines, in particular platform approaches that are based on mRNA or DNA. This effort is under a project called Medical Biological Defense - Advanced Component Development and Prototypes.[136]

In addition, the CBDP and USAMRIID should draw programmatic ideas from other organizations. A decade ago, DARPA funded Moderna to develop mRNA vaccines against a range of pathogens. DARPA is currently completing a successor to this program that uses genetic material, such as mRNA, to compel the human body to produce antibodies tailored to specific pathogens.[137] These gene-encoded antibodies can serve as treatments for patients and also provide temporary protection akin to vaccination but shorter-lasting.[138] CBDP and USAMRIID should consider serving as transition partners for this program. CBDP is already investing heavily in a related approach that has significant challenges for scaling up manufacturing (monoclonal antibodies). As such, also investing in gene-encoded approaches makes sense. USAMRIID in particular could be helpful for using this platform to develop gene-encoded antibodies against high-fatality pathogens.

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134 U.S. Department of Defense - Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission," This finding is based on CSR's review of approximately 30 DoD budget documents at the source above, in particular the procurement and research, development, test and evaluation submissions for the CBDP from 2005-2021.

135 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2017-2021 Program and Budget Review Submission," (Washington, DC: U.S. Government Publishing Office, 2021).

136 Ibid.

137 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "Defense Advanced Research Projects Agency, Defense-Wide Justification Book Volume 1 of 5, Research, Development, Test & Evaluation," (Washington, DC: U.S. Government Publishing Office, 2021).

138 U.S. Department of Defense - Defense Advanced Research Projects Agency, "ADEPT:PROTECT," 2021.

CONGRESS SHOULD REQUIRE A GAO REPORT ON TALENT CHALLENGES

Scientists are driven by their curiosity and pride themselves on the creativity and ingenuity of their solutions. Top USAMRIID scientists should be helping to set research agendas, in addition to implementing them. Many of the institute's challenges, including loss of talent, stem from this underlying problem.

At the same time, in recent years the U.S. Army has curtailed the professional development of infectious disease specialists. USAMRIID has switched to a contractor model that has contributed to job insecurity. Today, there are 300 contractors and 500 employees at the institute, a stark change from the 1990s when there were two contractors in total on the payroll.[139] These contractors are employed to support specific CBDP projects, and so as the CBDP budget has been cut, many have been dismissed. The pauses in activity that have occurred over the last few years have accelerated this trend. For example, in November 2019, when the COVID-19 outbreak was beginning, the CDC temporarily shut down projects associated with USAMRIID's high containment laboratories, leading to thirty contractors being laid off right when they were needed most.[140]

The overall result—between a reduction in USAMRIID's independence and a shift to contracting—has been a deterioration of morale and a loss of talent at the top biodefense laboratory.

The necessary but major changes proposed above to redefine the institute's mission and grant it more independence are intended, in part, to make USAMRIID a more attractive employer for top biodefense scientists and researchers. But these changes also introduce uncertainty for USAMRIID's elite cadre of biodefense experts. To ensure USAMRIID's talent is maintained through these changes, Congress should require a GAO report on USAMRIID talent to inform future legislation regarding the institute. That way, Congress can stay better informed of the personnel challenges at USAMRIID and also be in a position to take action---and can help ensure that attracting top talent is part of the potential mission and organizational shifts described above. Congress may also consider requesting follow-on GAO reports, including those tracking the effects of any significant changes to USAMRIID.

CONCLUSION

USAMRIID is the premier U.S. biodefense laboratory, and it should be a key source of ingenuity and leadership in accomplishing the goal of making this pandemic the last, and addressing biological weapons threats. However, the U.S. government is not utilizing USAMRIID to its full potential and current funding mechanisms are depleting it of expertise. There are deep problems with USAMRIID that this analysis has sought to bring to the attention of policymakers. There are also achievable solutions, beginning with considering an expanded mandate and a different model for USAMRIID that would give the top biodefense experts in the world the intellectual freedom to seek out creative approaches to the many biological threats the United States faces.

139 David R. Franz and Judith Miller, "A Biosecurity Failure," *City Journal*, 2020.

140 Ibid.

U.S. Department of Health and Human Services Headquarters. Department of Health and Human Services.
CHRISTOPHER E. ZIMMER/SHUTTERSTOK

THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

On August 23, 2021, the world reached the latest in a series of significant milestones concerning vaccines: the U.S. Food and Drug Administration (FDA) gave full approval of the first COVID-19 vaccine for use in individuals 16 years of age and older.[141] This mRNA-based vaccine approval came as the global community was struggling to contain and control the transmission and tragedies arising from the highly infectious delta variant of SARS-CoV-2.[142]

The U.S. Department of Health and Human Services (HHS) has played an integral role in bringing safe and effective vaccines into use in record time, and just about every other aspect of the COVID-19 pandemic response. This builds on its history of responses to past biological events that the United States and the international community have faced.[143]

141 U.S. Food and Drug Administration, "FDA Approves First COVID-19 Vaccine: Approval Signifies Key Achievement for Public Health," August 23, 2021.

142 Marc Santora and Isabella Kwai, "Known Global Toll Reaches 200 Million Virus Infections," *The New York Times*, August 4, 2021.

143 For examples, see United States Department of Health and Human Services, Assistant Secretary for Preparedness and Response, *Ebola Response Improvement Plan: Based on Lessons Learned from the 2014 - 2016 Ebola Epidemic*, 2016; U.S. Department of Health and Human Services, Public Health Emergency, "Middle East Respiratory Syndrome Coronavirus (MERS-CoV)," 2013; U.S Department of Health and Human Services, *An HHS Retrospective on the 2009 H1N1 Influenza Pandemic to Advance All Hazards Preparedness*, June 15, 2012; and U.S. Government Accountability Office, *Report to the Honorable Bill Frist, Majority Leader, U.S. Senate on Bioterrorism: Public Health Response to Anthrax Incidents of 2001*, 2003.

HHS contains unique capabilities for addressing the biological threats to humans, animals, agriculture, and the environment that the United States faces. How HHS addresses biological threats, including deliberate biological attacks against U.S. citizens, has also significantly changed in the post-2001 era.[144] This section focuses first on two of the most important entities that stemmed from these changes, which are central to the U.S. ability to mitigate the most catastrophic biological risks:

- The formation of an entirely new office within HHS—the Office of the Assistant Secretary for Preparedness and Response (ASPR)—to lead the effort on preparing for, responding to, and recovering from disasters and public health emergencies, which include the entire spectrum of biological threats that affect U.S. citizens.[145]

- The creation of the Biomedical Advanced Research Development Authority (BARDA), a core component housed within ASPR that plays a significant role in addressing public health and medical emergencies caused by natural and deliberate sources.

ASPR and BARDA constitute a major step forward in the U.S. ability to address biological threats. They house crucial expertise, leadership functions, and authorities for fostering public-private collaboration to revolutionize the technologies used in public health disaster responses and steady-state conditions.

Following the sections on ASPR and BARDA, this chapter provides an overview and recommendations regarding the National Institutes of Health (NIH). Housed within the Department of Health and Human Services, the NIH is one of the nation's leading scientific agencies and conducts significant work related to biodefense and biological threat reduction.

THE OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE (ASPR) AND THE BIOMEDICAL ADVANCED RESEARCH DEVELOPMENT AUTHORITY (BARDA)

Two back-to-back attacks in 2001--- the 9/11 terrorist attacks and the anthrax dispersion and distribution through the U.S. Postal Service---forced a paradigm shift in how the United States considered national security and public health issues. Significant threats to the U.S. homeland, including through the use of biological weapons, was no longer theoretical, but had become a lived experience---a new reality.[146]

The United States government took a significant series of actions to address the emergence of these new threats. One major action amended the Public Health Service Act, which is the federal law that directs federal preparedness concerning public health emergencies. This amendment, passed in 2006, was the Pandemic and All-Hazards Preparedness Act (PAHPA). It did three main things to improve the U.S. ability to prepare for and respond to public health and medical emergencies from natural or anthropogenic sources.[147]

144 Gigi Kwik Gronvall, "Biodefense Countermeasures: The Impact of Title IV of the U.S. Pandemic and All-Hazards Preparedness Act," *Emerging Health Threats* Vol. 1, No. 1, 2008: p. 7073.

145 U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response, *Strategic Plan for 2020 - 2023*, 2020.

146 Christopher Wray, "The FBI and the National Security Threat Landscape: The Next Paradigm Shift," *FBI*, April 26, 2019.

147 Please see U.S. Food and Drug Administration, "MCM-Related Counterterrorism Legislation," 2021, and Eric D. Hargan and Robert Kadlec, "It Took Years to Reach Vaccine Warp Speed," *Wall Street Journal*, 2021.

First, PAHPA led to the establishment of a new leadership team within the Office of the Secretary at HHS: the Office of the Assistant Secretary for Preparedness and Response (ASPR). This office serves as the principal advisor to the HHS Secretary on issues concerning preparedness and response for federal public health and medical matters.[148]

Second, PAHPA established the Biomedical Advanced Research and Development Authority (BARDA) within the newly-established ASPR office. BARDA was established as a way to address shortcomings from the enactment of the Project BioShield Act of 2004, which was meant to foster coordination and collaboration between HHS and the private sector for both the development of medical countermeasures against chemical, biological, radiological, and nuclear threats and the acquisition of such countermeasures for stockpiling purposes.

Third, PAHPA increased federal funding for state and local public health preparedness. Some of this funding also went to programs like the Centers for Disease Control and Prevention's (CDC's) Public Health Emergency Preparedness cooperative agreement grant program to strengthen state and local biological laboratory capacities, accelerate the identification of certain pathogens, and build the infrastructure necessary to quickly respond in the event of a public health event.[149]

ASPR AND BIOLOGICAL THREATS

The Office of the Assistant Secretary for Preparedness and Response (ASPR) works toward addressing biological threats through activities driven by four main goals: fostering strong leadership, sustaining a robust and resilient public health security capacity, building a regional disaster health response system, and advancing an innovative public health emergency medical countermeasure enterprise.[150]

In terms of fostering strong leadership, ASPR often leads or supports development, coordination, and implementation initiatives that deal with the public health and medical aspects of emergent threats such as biological events.[151] For example, ASPR is the operational lead for Emergency Support Function 8 within the National Disaster Response Framework. This means that ASPR is responsible for the coordination of national public health preparedness, and responses to and recovery from outbreaks and natural disasters. This work spans health surveillance, all-hazard public health and medical consultation, technical assistance and support, public health and medical support, vector control, and more.[152] ASPR also leads interagency coordination in implementation and evaluation for strategies like the National Biodefense Strategy.[153]

For sustaining a robust and resilient public health security capacity, ASPR focuses on identifying the people, processes, systems, and capabilities that would allow the United States to most optimally address a wide range of anthropogenic and naturally-occurring biological threats and hazards. Since October 2018, ASPR has served as the oversight office of the Strategic National Stockpile (SNS), and has been charged with increasing the operational effectiveness and

148 Ryan Morhard and Crystal Franco, "The Pandemic and All-Hazards Preparedness Act: Its Contributions and New Potential to Increase Public Health Preparedness," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* Vol. 11, No. 2, 2013: pp. 145 - 152.

149 Ibid.

150 U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response (ASPR), "HHS Office of the Assistant Secretary for Preparedness and Response," 2021.

151 U.S. Department of Health and Human Services, ASPR, *Pandemic and All-Hazards Preparedness Act Progress Report*, 2007.

152 U.S. Department of Health and Human Services, Federal Emergency Management Agency, *Emergency Support Function #8 - Public Health and Medical Services Annex*, 2008.

153 U.S. Department of Health and Human Services, ASPR, *Strategic Plan for 2020 - 2023*, 2020.

efficiencies of the SNS. This stockpile started in the Clinton era, and expanded under President George W. Bush, and can distribute large quantities of medicine, medical supplies, and personal protective equipment in the event of a public emergency.[154] Congress deemed the 2018 oversight transfer from CDC to ASPR as logical given ASPR's in-house capabilities and mission related to medical countermeasure development and acquisition via BARDA.

ASPR is also focused on public-private partnerships and finding new ways to innovate. Such efforts include the development of a Foundry for American Biotechnology - a collaboration between ASPR's Program Office for Innovation and Industrial Base Expansion and innovative technology centers like the Advanced Regenerative Manufacturing Institute. This collaboration is meant to spur biotechnology innovation by offering an all-in-one space for regional experts to form ideas, test them in dry and wet lab spaces, and develop proof-of-concept and novel products through in-house manufacturing capabilities.[155]

Further, ASPR helps coordinate key players, address gaps, and ensure that federal, state, local, tribal, and territorial governments have the necessary capabilities in advance of a public health emergency.[156] To build a regional disaster health response system, ASPR realizes that the challenges of man-made and naturally-occurring threats can happen across broad geographies with differing levels of capabilities, capacities, and resources. Therefore, this Office focuses on taking several pathways to generate a unified approach that improves healthcare readiness and medical surge capacity. One pathway is to modernize the National Disaster Medical System such that the all-hazards disaster healthcare system can be integrated into hospitals, emergency medical services, and public health agencies. In the case of a public health emergency, this integration can be critical to minimize disruption and excess surging that could overwhelm hospitals and other healthcare facilities. Another pathway is to strengthen existing supply chains for medical materials in advance of emergency events through increased engagement and cooperation with the private sector.[157]

Within ASPR, the Biomedical Advanced Research and Development Agency (BARDA) directly addresses biological threats by overseeing and managing the development and acquisition of medical countermeasures and diagnostics with the aim of fostering revolutionary advances in these fields. BARDA is unique in its public-private collaboration: in addition to providing funding, it helps companies develop partnerships that they need to advance new technologies faster and more effectively, provides subject matter expertise and support, and even communicates key information to the private sector through outreach events like BARDA Industry Day.[158]

When BARDA was initially established by Congress in 2006, it received $200 million in funding for FY2007 - FY2008 to accomplish its mission. In subsequent years, funds from Project BioShield were reallocated to BARDA in the form of a Special Reserve Fund. The returns on this small investment in facilitating and accelerating medical countermeasure research, development, licensure, and acquisition demonstrated the incredible value of BARDA's approach: 30 projects that were supported under Project BioShield, the introduction of 18 products to the Strategic National Stockpile to address CBRN threats, and the successful navigation of 22 products that were licensed or approved for use by the U.S. Food and Drug Administration.[159]

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154 U.S. Department of Health and Human Services, ASPR, "Products - Strategic National Stockpile," August 9, 2021.

155 Ana Mulero, "HHS Launches Foundry for American Biotechnology to Spur Innovation," *PharmaNews Intelligence,* 2020.

156 ASPR, *Strategic Plan for 2020 - 2023*.

157 Ibid.

158 Ibid.

159 For examples, see Bradley T. Smith, Michael Mair, Gigi Kwik Gronvall, and Jason Matheny, "Developing Medical Countermeasures for Biodefense," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* Vol. 7, No. 1, 2009: pp. 42 - 43 and U.S. Department of Health and Human Services, ASPR, "Project Bioshield and Overview of Key Accomplishments," 2019.

Most recently, BARDA was a key component in Operation Warp Speed (OWS): an interagency partnership between HHS and the Department of Defense (DoD) that sought to accelerate the development of promising vaccine and therapeutics candidates with private sector partners to address the COVID-19 pandemic. (OWS is examined in greater depth in *Part VI* of this handbook.) BARDA played a number of critical roles during this partnership, including early funding, development, and deployment of COVID-19 test kits and the successful acceleration and navigation of promising vaccine candidates to emergency use authorization and fully-licensed statuses.[160]

BARDA'S PROJECT BIOSHIELD AND PAN-INFLUENZA PROGRAMS

Among the programs that BARDA oversees today, two are particularly noteworthy for creating the strong bio-industrial base needed to prevent future pandemics and encourage U.S. companies to contribute to national security needs: Project BioShield and "pan-influenza" projects.

The Project BioShield Act was signed into law in 2004 and enables the government to fund the development, acquisition, and stockpiling of medical countermeasures needed to protect the U.S. population from weapons of mass destruction.[161] Project BioShield is managed by BARDA. Since its establishment, the program has focused on building partnerships with biotechnology and pharmaceutical companies to incentivize the production of vaccines, therapeutics, diagnostics, and other relevant technologies. To facilitate these partnerships, Project BioShield grants NIH/NIAID the authority to award grants and contracts in a streamlined, accelerated manner.[162]

In addition to promoting cutting-edge research and development, the program also establishes a secure funding source for the government to purchase medical countermeasures, known as a Special Reserve Fund. This incentivizes providers to actually develop the products the U.S. government determines to be important for national security purposes, as they can have higher confidence that what they develop will be purchased.

The Project BioShield Act also establishes Emergency Use Authorization (EUA), through which the FDA Commissioner can authorize the use of as-yet-unapproved medical products in emergencies. This authority has proven incredibly important in the COVID-19 pandemic, as it allowed expedited access to life-saving vaccines.[163] Project BioShield plays a key role in advancing the development and deployment of medical countermeasures, making it a crucial piece of the biosecurity enterprise.

BARDA has several programs designed to prepare the United States for influenza outbreaks of pandemic potential. The core focus of the "pan-influenza" programs is to promote the development of effective and rapidly scalable medical countermeasures that will aid in preventing or attenuating influenza pandemics.[164] Vaccine modernization is a central priority, including developing alternate delivery mechanisms, optimizing adjuvants, and improving on recombinant flu vaccines. To achieve these goals, BARDA works closely with industry, fostering innovation through public-private partnerships.

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160 For examples, see U.S. Department of Health and Human Services, Public Health Emergency, "Response Dashboard," 2021; U.S. Department of Health and Human Services, Public Health Emergency, "BARDA COVID-19 Response Timeline,", 2021; *Congressional Research Service Report: COVID-19 Vaccines and Ancillary Vaccination Materials*, 2021; and Agata Dabrowska, Frank Gottron, Amanda K. Sarata, and Kavya Sekar, *Congressional Research Service Report: Development and Regulation of Medical Countermeasures for COVID-19 (Vaccines, Diagnostics, and Treatments): Frequently Asked Questions,* June 25, 2020.

161 U.S Department of Health and Human Services, Public Health Emergency, "Project Bioshield," May 19, 2021.

162 U.S. Department of Health and Human Services, "Project Bioshield Overview," *Medicalcountermasures.gov.*

163 U.S Food and Drug Administration, "COVID-19 Vaccines," November 19, 2021.

164 U.S. Department of Health and Human Services, Public Health Emergency, "BARDA's Pandemic Influenza Programs," May 3, 2021.

A box of the COVID-19 treatment Paxlovid. ASPR's Biomedical Advanced Research and Development Authority concluded a purchase agreement with Pfizer for the U.S. government to receive 10 million treatment courses of Paxlovid, an investigational drug that reduces mortality from COVID-19 by 90%. RARRARORRO/SHUTTERSTOCK

In addition, these programs seek to expand domestic manufacturing capacity to enable a quick response when a surge of production is needed. A major emphasis across BARDA's pan-influenza programs is taking a proactive rather than reactive approach—setting up the infrastructure in advance enables an immediate response when a threat is detected. These programs are instrumental in preparing for influenza pandemics, whether the virus is naturally arising or weaponized.

RECOMMENDATIONS

ASPR has made significant progress in addressing biological threats. Further, it has managed to make progress despite the office's relative youth and large mission-set that cuts across broad portions of the interagency. This office, like others across the interagency, has had its share of growing pains, including insufficient oversight of proper use of funding and questions about the balance of investments across solutions for addressing naturally-arising disease threats, deliberate biological weapons threats, and those that cross the full spectrum of biological risks.[165]

Additionally, the challenges the United States has faced with the COVID-19 pandemic show that leveraging ASPR and BARDA to their full potential will require sustained resources and answers to several critical questions. We therefore recommend the following steps.

165 U.S. Office of Special Counsel, "HHS Misused Millions of Dollars Intended for Vaccine Research, Emergency Preparedness," 2021.

First, the evolving character of natural and deliberate biological threats means that the United States **must begin moving past its mostly list-based system of addressing biological threats to one that better accounts for the emergence of novel health threats.** The current way that ASPR, BARDA, and the entire federal government deal with biological threats is built on a list-based system: through information exchange and analysis across the interagency, HHS is required to establish and regulate a list of biological agents and toxins that have the potential to pose a severe threat to public health and safety.[166] While this does help prioritize and focus efforts on a finite number of high-risk pathogens, it ignores the possibility that novel pathogens from natural and anthropogenic sources beyond the list may wreak havoc on the United States and the globe, as we have recently seen.[167]

Continuing a trend that is already beginning, the United States needs to keep investing in countermeasures, diagnostics, and pathogen detection capabilities that cross many diseases. This is in progress, as seen by the United States starting to pivot to platform technologies, genomic surveillance, multipurpose detection and diagnostic tools, and initiatives like BARDA's investment in pan-influenza solutions.

Johns Hopkins University's Center for Health Security has developed a novel framework known as the Disease X Medical Countermeasure Program that would significantly augment the current U.S. approach to addressing biological threats. This framework embraces the uncertainty of when the next pandemic will occur, and prepares against the fact that infectious disease outbreaks now occur 3 times more often than 40 years ago. It would focus on medical countermeasure efforts to address threats from viral families that are most likely to cause pandemics, as opposed to historic, limited approaches such as the "one bug, one drug" approach of developing countermeasures effective against single pathogens.

Such efforts, particularly leveraging technologies and vaccine platforms available and accessible through ASPR and BARDA, would directly increase U.S. safety and security from catastrophic biological threats. Rather than focusing on a finite list-based threat assessment, this effort would develop methods to accelerate novel antiviral therapies against currently-unknown viral threats.[168] Continuing movement in this direction is also crucial to deterring actors who may seek to weaponize diseases that narrowly-focused medications and detection tools might not address. Further, programs like the Disease X Medical Countermeasure Program can help the United States avoid the enormous economic impacts from events like COVID-19, from which the nation has lost $500 billion for each additional month the pandemic has continued.[169]

Second, ASPR and BARDA should also **help ensure connectivity across pathogen early warning and the development of new diagnostics and countermeasures.**

After significant advances over the past few decades, biosurveillance and early warning systems for potential outbreaks have proven highly useful in local public health responses but insufficient to get ahead of some types of infectious diseases like COVID-19. ASPR and HHS broadly worked hard to remediate issues in timely data sharing during the pandemic, including through the use of new tools and requirements for states to improve information-sharing to the federal level. That progress needs to be sustained.

Looking forward, ASPR will likely play a key role in setting the stage for a highly-prepared bioeconomy and ensuring improved data collection and sharing for effective early warning. As such, ASPR and BARDA leaders should be sure

166 CDC and USDA, "Select Agents and Toxins," 2020.

167 National Academies of Sciences, Engineering, and Medicine, *A Strategic Vision for Biological Threat Reduction: The U.S. Department of Defense and Beyond,* (Washington, DC: The National Academies Press, 2020).

168 Johns Hopkins Center for Health Security, "Johns Hopkins Center for Health Security Commends U.S. Senators Baldwin, Casey, King, and Smith for Introducing the Disease X Act to Respond to Future Viral Outbreaks," 2021.

169 Johns Hopkins Center for Health Security, "Disease X Medical Countermeasure Program," 2021.

to coordinate with the new Center for Disease Forecasting and Outbreak Analytics,[170] which will be housed under the CDC yet require whole-of-government data and collaboration. In particular, ASPR and BARDA can help ensure data standards and interoperability for early warning as it fosters new diagnostic and detection tools---and in ensuring that new U.S. forecasting and early warning systems produce the types of data that are required for rapidly developing countermeasures and diagnostics early in a potentially-grave outbreak.

Finally, **ASPR and BARDA should continue strong collaboration with DoD in a post-Operation Warp Speed world.** Each side brings complementary expertise and strengths that, when combined, can produce incredible results. The rapid development, testing, production, scaling, and distribution of highly effective and safe vaccines for COVID-19 within 1 year was an unprecedented feat given that vaccines typically take 10 - 15 years to develop from start to finish.[171] Further, BARDA and DoD collaborated in other ways, including joint awards to increase the production and access of critical ancillary supplies for vaccine administration, including maximizing the availability of needles and syringes.[172] Finally, while BARDA successfully brought promising vaccine candidates to various states of licensure, it needed the logistics and production capabilities of DoD to make OWS the success that it is.[173]

ASPR and its biomedical component, BARDA, have the potential to forge new, effective paths forward in addressing catastrophic biological risks. Taking advantage of the latest technologies, building robust data streams and analytics, and better engagement across the interagency and with private sector partners can catalyze these entities to make the U.S. safer and more secure from the rapidly-evolving landscape of biological threats that the United States and the global community face.

170 CDC, "CDC Stands Up New Disease Forecasting Center," 2021.

171 Mark Toshner, "Less Than a Year to Develop a COVID Vaccine - Here's Why You Shouldn't Be Alarmed," *The Conversation,* 2020.

172 U.S. Department of Health and Human Services, "From the Factory to the Frontlines: The Operation Warp Speed Strategy for Distributing a COVID-19 Vaccine," 2020.

173 C. Todd Lopez, United States Department of Defense, "Defense Experience, Capabilities Further 'Herculean' Operation Warp Speed Efforts," 2020.

TOOLS OF THE TRADE: THE STRATEGIC NATIONAL STOCKPILE

The Strategic National Stockpile (SNS) is an inventory of medical supplies maintained by the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) under HHS ASPR. It is intended to protect Americans in case of a public health emergency, natural disaster, or chemical or biological weapons attack. The stockpile includes ventilators, personal protective equipment, antibiotics, vaccines, emergency medications, and other medical resources.[174]

The response to the COVID-19 pandemic revealed some significant shortcomings in the Strategic National Stockpile. Governors who requested materials from the stockpile found that the process was inefficient and that their needs were not filled in a timely manner—the stockpile was strained by requests for its use by all 50 states at once.[175] In addition, the process of scaling up production for masks, gloves, and surgical gowns was slow, and there were severe shortages months into the pandemic.

It is time to re-envision how the United States considers the utility of the Strategic National Stockpile, and how it pursues that vision. The SNS should lay the groundwork for the partnerships, training, manufacturing, and distribution that are necessary in crises, in addition to amassing key materials. This will allow the SNS to be leveraged as a means of creating and maintaining a vibrant bio-industrial base for the benefit of public health, economic security, and national security—and viewed as a critical element of U.S. deterrence against biological weapons.

Dr. Monique K. Mansoura, Executive Director for Global Health Security and Biotechnology at The MITRE Corporation, described this vision in a CSR webinar on October 27, 2021:

> "The value of a stockpile is not only the vaccines, or whatever is in the stockpile, it's how we got there. How did we make it? What did we learn? Who did we train? That is a part of the inter-crisis business model…If we want a speed element in our portfolio, and we do, for threats both known and unknown, we need to practice. . .You actually run the drill, and you learn a lot. You realize there might be capabilities you need where businesses need to make partnerships. Businesses are good at that, they do this every day. If they need a capability, they know how to find it. If the government can facilitate or support that, that's an important role for the government to play."[176]

In this vision, the stockpile is a tool for national preparedness and a strong industrial base, which would in turn promote economic health and support other national objectives as well. This also means that the SNS should strike a balance between accumulating universally useful materials and serving as a means of fostering a flexible, dynamic approach to scaling up production when a crisis strikes. The latter role may gain even more emphasis over time, as traditional stockpiling can be limiting. For instance, storing enough N95 masks for the entire population in preparation for an outbreak would fill every warehouse in the nation.[177] A practical approach is to have manufacturing capabilities in place to enable rapid scale-up of the medical supplies needed and exercise the distribution lines needed. Such a bio-industrial base can be supported by the exercises outlined in *Part VI* of this handbook, and by continually supplying the SNS. This way when an emergency response is needed, manufacturing can quickly and seamlessly ramp up.

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174 U.S. Department of Health and Human Services, "Strategic National Stockpile," 2021.

175 Shira Stein, "The Future of the U.S. National Stockpile Isn't a Bigger Stockpile," *Bloomberg*, December 10, 2020.

176 Christine Parthemore, Andrew Weber, Matt Hepburn, and Monique K. Monsoura, "Operation Warp Speed: The Interagency and Public-Private Collaborations that Drove It," YouTube Video, 58:47, October 27, 2021.

177 Stein, "The Future of the U.S. National Stockpile," 2020.

Members of the Oklahoma National Guard walk in a Strategic National Stockpile warehouse.
Tech. Sgt. Kasey Phipps/Oklahoma Army National Guard

To enable surge capacity, the government needs to maintain sufficient market intelligence, including on what the private sector is capable of producing and how quickly supplies can be purchased. In addition, the government should build partnerships with suppliers in the private sector that can be called upon in times of crisis. These partnerships should include large, well-established companies as well as smaller companies that can often uniquely bring agility and innovation.[178]

Security of supply chains is also a key concern for PHEMCE to consider with regard to the stockpile. The COVID-19 pandemic highlighted U.S. reliance on global supply chains that were not able to meet demands.[179] Creating more domestic manufacturing capabilities would shore up supply chains and ensure that the U.S. government can achieve surge capacity when needed, regardless of relationships with other nations.

Sustained funding of the SNS is crucial to its success. By smartly choosing resources to stock up on, and putting greater emphasis on enabling surge capacity through public-private partnerships and market intelligence, the SNS can be a more effective resource.

As the SNS potentially takes such new directions in the future, one thing is certain: it will play a starring role in deterring biological weapons threats in addition to its public health utility. One example can be seen in the fact that the stockpile contains 300 million doses of smallpox vaccines, enough for almost all Americans.[180] The result of the efforts that drove this was to effectively take smallpox off the table as a mass destruction threat to the nation. The achievements behind the creation of smallpox vaccines and the foresight to use them in this way must be replicated in leveraging the stockpile for both preparedness and deterrence in the years ahead.

178 Christine Parthemore, Andrew Weber, Matt Hepburn, and Monique K. Monsoura, "Operation Warp Speed: The Interagency and Public-Private Collaborations that Drove It," YouTube Video, 58:47, October 27, 2021.

179 North Carolina State University, "The Strategic Stockpile Failed; Experts Propose New Approach to Emergency Preparedness," *ScienceDaily*, 2020.

180 Daniel M. Gerstein, *Testimony Presented before the Senate Committee on Homeland Security and Governmental Affairs—The Strategic National Stockpile and COVID-19: Rethinking the Stockpile*, June 24, 2020.

James H. Shannon Building (Building One), NIH campus, Bethesda, MD. Lydia Polimeni/ National Institutes of Health

THE ROLE OF THE NATIONAL INSTITUTES OF HEALTH IN ADDRESSING BIOLOGICAL THREATS

The National Institutes of Health (NIH) has played an instrumental role in health research since its inception over a century ago. As the largest public funder of biomedical research in the world, the NIH has great influence over the research priorities that scientists choose, as well as attitudes, research practices, and safety standards in the United States and around the world.[181] This power to drive the direction of science can be leveraged to encourage productive and safe research that will advance U.S. biosecurity goals. The National Institute of Allergy and Infectious Diseases (NIAID), an institute of NIH, is particularly relevant in this space, as the research it conducts on emerging diseases, therapeutics, and other areas is directly pertinent to defense against all biological threats.

The NIH receives a large portion of total biodefense and biosecurity-related research and development funding. As such, it has a great responsibility to contribute substantially to biological defense. This section will examine how to maximize the NIH's impact in this space. Core focus areas for the NIH are ensuring that it funds work with high impact potential, limits dangerous dual-use research, improves transparency in spending, and commits to interagency collaboration for transitioning efforts it funds to commercialization when such advances are possible.

181 U.S. Department of Health and Human Services, National Institutes of Health, "Impact of NIH Research," 2018.

Dr. Francis Collins, until late 2021 the Director of the National Institutes of Health (NIH), holds up a model of COVID-19, known as coronavirus, during a Senate Appropriations subcommittee hearing on the plan to research, manufacture and distribute a coronavirus vaccine, known as Operation Warp Speed, Thursday, July 2, 2020, on Capitol Hill in Washington.
Saul Loeb/Pool via AP

ENSURING IMPACT

In order to optimize the utility of the NIH and NIAID, it is essential that the agencies prioritize conducting innovative work with high impact potential, even if that work is not guaranteed to succeed.

This is not always the case today. The NIH is viewed by some as overly risk-averse, and recently its ability to conduct groundbreaking research has been questioned.[182] In the past couple of decades, the NIH has become less likely to fund work that builds on very recent ideas, instead delaying such investments.[183]

Yet such investments in cutting-edge research are key to driving rapid progress. Incremental advances are not enough to keep pace with the growing risk of biological threats. The NIH has seen the importance of pushing more toward higher-reward efforts and currently runs several funding programs to encourage it.[184] Increasing the funding and emphasis on this type of program would be an excellent path for NIH to ensure that it is promoting scientific progress at the fastest rate possible, which is crucial after the devastation of the COVID-19 pandemic.

In addition to ensuring that work is not too risk-averse, it is important to consider what research topics will be most productive or impactful and set priorities accordingly. Roadmaps developed by experts in the field can serve as a guide

182 Jocelyn Kaiser, "Biden Wants $6.5 Billion for New Health Agency to Speed Treatments," *Science*, 2021.

183 Mikko Packalena and Jay Bhattacharya, "NIH Funding and the Pursuit of Edge Science," *PNAS* Vol. 117, No. 22, 2020: pp. 12011-12016.

184 National Institutes of Health, Office of Strategic Coordination, "High-Risk, High-Reward Research," 2021.

on where the NIH/NIAID should be committing resources.[185] Increasing focus should include work that can contribute to addressing both known threats and, looking to the future, emerging pathogens and biological weapons risks.

One critical piece of such work is focusing on rapid response platform technologies that can be used for addressing both known and novel biological threats. The success of the mRNA vaccine for COVID-19 is evidence of the utility of platform technologies. Another is medical countermeasures that can be used to counter a wide variety of biological threats, rather than disease-specific solutions.[186]

RAPID ACCELERATION OF DIAGNOSTICS (RADX) INITIATIVE

In April 2020, the NIH launched the Rapid Acceleration of Diagnostics (RADx) initiative with the goal of speeding the development and implementation of COVID-19 testing.[187] RADx uses a streamlined, competitive process to select promising technologies for funding, and supports scientists as they move through stages of development and commercialization. The initiative has been highly successful: the first teams selected for funding were able to deliver millions of validated COVID-19 tests within months.[188] New technologies are continually being added to the program, focusing on lowering costs and increasing accessibility and performance.[189]

Interagency collaboration has been key to the success of RADx, particularly with BARDA—the two HHS agencies have worked together to fund projects, and BARDA has provided support with later stage development.[190] In addition, RADx has demonstrated how much the private sector can contribute when strong public-private partnerships are fostered. The initiative attracted some of the most innovative companies from the United States and around the world.

RADx is a valuable example of an initiative at the NIH that encouraged rapid turnaround, innovative techniques, and a collaborative process. Even when the COVID-19 pandemic wanes, RADx can continue to contribute to improving U.S. diagnostic capabilities. Investments in platform diagnostics, as well as multiplexed diagnostics that can detect multiple pathogens at once, should be a focus for RADx moving forward. Moreover, having rapidly accessible testing is crucial to pandemic early warning — if early cases are detected and reported, contact tracing can prevent mass infections. Such an early warning system requires tying together diagnostics and data reporting. This would be a valuable direction for RADx to move in.

185 Engineering Biology Research Consortium, "Enabling Defense Applications through Engineering Biology," 2020.

186 Johns Hopkins Center for Health Security, "Center for Health Security Report Reviews the Promise and Challenges of Vaccine Platform Technologies," 2019.

187 U.S. Department of Health and Human Services, National Institutes of Health, "Rapid Acceleration of Diagnostics (RADx)," 2021.

188 Andrea Park, "What's Next for RADx? The NIH Drafts a To-Do List for its $1.5B Diagnostics Competition, Through COVID and Beyond," *Fierce Biotech*, 2021.

189 U.S. Department of Health and Human Services, National Institute of Biomedical Imaging and Bioengineering, "NIH RADx initiative expands COVID-19 testing innovation for additional types of rapid tests," Press Release, 2021.

190 U.S. Department of Health and Human Services, National Institutes of Health, "NIH RADx Initiative Advances Six New COVID-19 Testing Technologies," News Release, 2020.

LIMITING GAIN-OF-FUNCTION RESEARCH

In addition to aiding in addressing biological threats, the NIH/NIAID must ensure that they are not creating unwarranted biological risks in the process. Another major area of importance is therefore the NIH's role in funding gain-of-function research, which is research that confers enhanced pathogenicity or transmissibility to dangerous pathogens. Gain-of-function research can be highly risky, as there is always a possibility of the accidental release of these especially harmful pathogens.[191]

Currently, HHS uses a framework to determine whether specific gain-of-function research is relatively safe to fund.[192] The Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO) allows for some gain-of-function research to be funded as long as it complies with strict biosafety regulations, and as long as there is no safer way to get the results.

The framework indicates that decisions on funding gain-of-function will be advised by a panel of experts. However, the names of members of this panel, as well as their deliberations, are not available to the public. Furthermore, the panel is limited to an advisory capacity, and is often not even consulted to review potentially risky research proposals. In order to effectively screen research, the panel must be consulted more frequently and the deliberative process must be made public—transparency is crucial.[193] In addition, the U.S. government should commit to ongoing evaluation of the HHS P3CO Framework to ensure that it stays up to date and maintains stringent standards, and is flexible enough to adapt to changes in molecular and synthetic biology.[194]

The P3CO Framework only applies to work funded by the NIH and other HHS agencies. U.S. policies regarding dual-use research in general are fragmented, and only apply to research that receives federal funding.[195] Additionally, there are limited mechanisms through which scientists can engage with the national security community. The NIH, as the leading institution on biological sciences in the United States, should commit to playing a greater role in setting the agenda on biosecurity and biosafety in research. One way of achieving this is to better leverage the National Science Advisory Board for Biosecurity (NSABB), which sits under the NIH. The NSABB is a federal advisory committee that provides recommendations and guidance on biosecurity concerns when requested by the U.S. government.[196] Currently, however, knowledge of the NSABB in scientific communities is limited, and the board has limited authority. The NSABB cannot restrict the publication of research that could be misused by malicious actors, only recommend against it.[197] An expanded mandate for NSABB could make this board more useful in shaping, promoting, and enforcing biosecurity in research.[198]

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191 David Willman and Madison Muller, "A Science in the Shadows," *Washington Post,* 2021.

192 United States Department of Health and Human Services, *Framework for Guiding Funding Decisions About Proposed Research Involving Enhanced Potential Pandemic Pathogens*, 2017.

193 Thomas Inglesby and Marc Lipsitch, "Proposed Changes to U.S. Policy on Potential Pandemic Pathogen Oversight and Implementation," *American Microbial Society: Synthetic Biology* Vol. 5, Issue 1, 2020: pp. e00990-19.

194 Salil Gunashekar, Sarah Parks, Joe Francombe, Camilla d'Angelo, Gemma-Claire Ali, Pamina Smith, Daniela Rodriguez-Rincon, Marlene Altenhofer, and Gordon R. McInroy, *Oversight of Emerging Science and Technology: Learning from Past and Present Efforts Around the World*, (Santa Monica, CA: RAND Corporation Publishing, 2019).

195 National Academies of Sciences, Engineering, and Medicine, *Dual Use Research of Concern in the Life Sciences: Current Issues and Controversies* (Washington, DC: The National Academies Press, 2019): p. 4.

196 National Institutes of Health, Office of Science Policy, "National Science Advisory Board for Biosecurity."

197 David Brown, "Health & Science Federal Panel Asks Journals to Censor Reports of Lab-Created 'Bird Flu'," *Washington Post*, 2011.

198 National Academies, *Dual Use Research of Concern in the Life Sciences*: p. 6.

IMPROVE TRANSPARENCY IN SPENDING

NIAID currently receives the majority of U.S. government research and development spending on reducing biological threats---on the order of $2 billion per year over the last decade, with that amount steadily increasing to closer to $3 billion in the last several years.[199] It is imperative that this work be leveraged maximally, and that the organization's leaders take seriously their significant influence on science for addressing these threats, including biological weapons risks.

While sustained funding at NIAID is positive, the agency has shown a lack of transparency with regard to how money is spent, especially when compared to DoD agencies. Better accounting of where funding is going, along with evaluation of the impact of research, would be useful. The strong continued political support for NIAID makes the agency valuable in advancing biosecurity goals, but this is only possible with better transparency. Given the high budget, substantial results should be expected.

INCREASING INTERAGENCY COLLABORATION

To make the best use of NIAID and its resources, it is crucial that the institute promotes collaboration among agencies to ensure research efforts complement each other and are not duplicative. NIAID mainly conducts basic research, so having open lines of communication and streamlined processes to allow other agencies to carry forward their work is necessary. Interagency rivalries and differing approaches, particularly between defense and non-defense agencies, must be smoothed out—though some at NIAID don't see themselves as involved in the biosecurity sphere, they are essential to U.S. national security in this regard. The basic research conducted by NIAID must not simply sit unused, or millions of dollars of biodefense spending will have gone to waste. Transition work via collaboration with other agencies is key to ensuring NIAID's work more frequently advances to higher technological readiness and achieves commercialization.

The NIH and NIAID have an essential role to play in responding to biological threats. By optimizing their commitment to safe research, focusing on developing innovative technologies, and better collaborating with other agencies, they can improve their ability to advance biosecurity and biodefense goals.

199 U.S. Department of Health and Human Services, National Institutes of Health, "Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC) - Biodefense," accessed November 4, 2021.

THE ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH (ARPA-H)

In April 2021, the U.S. Executive Branch proposed the creation of the Advanced Research Projects Agency for Health (ARPA-H) within the NIH, requesting a budget of $6.5 billion.[200] The main aim of this agency would be to accelerate the pace of health sciences research and push for bold, innovative advances that can make it out of the lab and into the commercialization stage.[201] The existing mechanisms of NIH aren't conducive to this type of work, as NIH favors hypothesis-driven, incremental research, rather than the transformative but higher-risk research ARPA-H seeks to conduct. ARPA-H is largely modeled after DARPA, with highly-skilled program managers selecting projects rather than them being selected by a traditional NIH review process. ARPA-H will look to DARPA's example of streamlined processes, flexible hiring, and willingness to take risk with high-reward potentials, while making some adjustments to the operating model to make ARPA-H successful in the biomedical realm.

While ARPA-H's focus is likely to be broad, by speeding the process of securing grants and encouraging transformative research, ARPA-H has the potential to support work with high impact for biosecurity. However, this will only be achieved if ARPA-H successfully makes the culture shift that they envision. Carefully selecting leadership, perhaps someone from outside of the NIH with a fresh outlook, is key in securing an innovative environment that avoids falling back to an incremental, risk-averse culture.[202] Additionally, the concept paper for ARPA-H mentions an emphasis on broadly applicable platform technologies. This is a necessary focus to maintain to ensure research is as impactful as possible.[203] Finally, ensuring collaboration among HHS agencies (Food and Drug Administration, Center for Disease Prevention and Control, BARDA), as well as the broader scientific community (National Institute of Standards and Technology, Department of Energy, National Science Foundation, etc.) will be essential. This is especially true when it comes to transitioning research from early to later stages — partnerships are important in getting technologies to their final readiness stages.

If ARPA-H is able to recognize the immense threats posed by biological weapons and emerging diseases, and include in its portfolios technologies that can help address both, the agency could have great potential in this space. The devastating impacts of COVID-19 should incentivize investment into research preventing the same disastrous effects from occurring in the future, and ARPA-H could play a helpful role.

CONCLUSION

The U.S. Department of Health and Human Services plays a central role in addressing and responding to catastrophic biological threats. Its contributions to the COVID-19 response, including the rapid development of a highly effective vaccine, demonstrate the Department's capabilities and potential in this space. ASPR, BARDA, and the NIH must commit to leveraging their broad influence and funding to produce the medical technologies and infrastructure necessary for combating biological threats.

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200 Lisa Winter, "President Biden Proposes Creating Two DARPA-Like Agencies," *The Scientist*, 2021.

201 White House, *Advanced Research Project Agency for Health (ARPA-H): Concept Paper*, 2021.

202 Sarah Owermohle, "Skeptics Question if Biden's New Science Agency is a Breakthrough or More Bureaucracy," *Politico*, 2021.

203 White House, "White House and National Institutes of Health Release Report Summarizing the Listening Sessions with Stakeholders on the Proposed Advanced Research Projects Agency for Health," 2021.

Department of State Headquarters and Sign. Government Accountability Office File Photo.

THE U.S. DEPARTMENT OF STATE[204]

Addressing biological threats depends heavily on relationships. Progress for the United States and the world in this area requires strong human and intergovernmental connections to encourage transparency, maintain situational awareness, share best practices, and build capacity around the world for finding and stopping biological threats before they cause mass destruction.[205] In this context, the Department of State's critical activities include:

- Leading U.S. engagement in fora like the Biological Weapons Convention (BWC) and promoting norms against biological weapons.
- Building capacity with partner nations via the Biosecurity Engagement Program, which engages life scientists, government officials, non-governmental organizations, and other stakeholders to improve biosecurity, biosafety, and pathogen surveillance and response.[206]

204 Much of the text in this section is drawn directly from Jackson duPont, Yong-Bee Lim, Christine Parthemore, and Alexander Titus, "Key U.S. Initiatives for Addressing Biological Threats Part 4: The Department of State," Council on Strategic Risks, August 23, 2021.

205 David R. Franz, "With the Changing Biological Threat...Smart International Engagement Policy Would Lower Cost and Increase National Security," *Virtual Biosecurity Center,* 2012.

206 U.S. Department of State, Biosecurity Engagement Program, "Biosafety and Biosecurity," 2020; Kenneth Yeh, Jeanne Fair, Helen Cui, Carl Newman, Gavin Braunstein, Gvantsa Chanturia, Sapana Vora, Kendra Chittenden, Ashley Tseng, Corina Monagin, and Jacqueline Fletcher, "Achieving Health Security and Threat Reduction through Sharing Sequence Data," *Tropical Medicine and Infectious Disease* Vol. 4, No. 2, 2019: p. 78; and U.S. Department of State, Biological Engagement Program, "About Us," 2020.

- Working through more than 270 embassies, consulates, and missions worldwide to lead and support arms control and counterproliferation efforts, for example via the Proliferation Security Initiative that aims to stymie weapons of mass destruction proliferation efforts.[207]
- Collaborating with other U.S. agencies, including via the Biodefense Coordination Team (which identifies gaps, shortfalls, redundancies, and opportunities for better activity and resource alignment) and the National Science Advisory Board on Biosecurity.[208]

The flipside to State's operational strength highlights a significant challenge it must also navigate: operating effectively in regions where relationships are weak or non-existent, including with regard to currently-sanctioned nations like Russia, North Korea, and Iran.

This chapter focuses on several emerging ideas and gaps that the department can fill in the years ahead:

- Leveraging existing and emerging technologies to assist in attribution and verification of treaty compliance
- Enhancing multilateralism via tailored bio cooperation mechanisms
- Expanding diplomacy and programs for pathogen early warning
- Appointing a special envoy and increasing biorisk expertise

LEVERAGE EXISTING AND EMERGING CAPABILITIES AND TECHNOLOGIES FOR ATTRIBUTION AND VERIFICATION OF TREATY COMPLIANCE

Attribution and verification of compliance with treaties against biological weapons have been perennial problems for State and other institutions. Three main factors contribute to these issues.

First, variations in capabilities and infrastructure, as well as data collection, logging and sharing, pose significant challenges to accurate and timely pathogen detection.[209] Second, the life sciences exemplify the dual-use dilemma: the phenomenon where research, development, deployment, and advances in the life sciences can produce both positive and illicit applications which, thus, makes it "inherently difficult to control one [application] without inhibiting the other."[210]

Third, even if the preponderance of a biological event points to the deliberate use of a biological weapon by a state actor, attribution and verification attempts are muddied by both politics and the difficulty in separating treaty-prohibited from treaty-permitted activities due to the dual-use dilemma. Therefore, intent becomes a key factor that State and other actors need to ascertain in suspected cases of biological weapons use.[211] These issues also complicate approaches for countries wishing to actively demonstrate that they are complying with treaty requirements.

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207 U.S. Department of State, "Diplomacy: The U.S. Department of State at Work," 2021; Susan J. Koch, *Occasional Paper 9 - Proliferation Security Initiative: Origins and Evolution,* National Defense University Press, 2012.

208 U.S. Government Accountability Office, *National Biodefense Strategy: Opportunities and Challenges with Early Implementation*, Statement by Chris P. Currie and Mary Denigan-Macauley, 2020.

209 Natasha E. Bajema, William Beaver, and Christine Parthemore, *Toward a Global Pathogen Early Warning System: Building on the Landscape of Biosurveillance Today*, Council on Strategic Risks, 2021.

210 Gerald L. Epstein, "Preventing Biological Weapons Development Through the Governance of Life Science Research," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* Vol. 10, No. 1, 2012: pp. 17 - 37.

211 Jonathan B. Tucker, "Biological Weapons Proliferation: Reasons for Concern, Courses of Action," Stimson Center, 1998.

Assessing intent continues to be a major challenge due to the difficulties in fully understanding something that is inherently sociopolitical. However, part of this can be potentially overcome, over time, by **better leveraging the relationships that already exist within and between the State Department and the broader intelligence community** (IC) given the IC's potential role in biological weapons detection, attribution, and verification.[212] The relationships within and between State and the broader IC can be further maximized by ensuring that all parties prioritize the countering-biological weapons mission, and that they are resourced accordingly. This will also best position the IC to support the U.S. delegation to the BWC in formulating U.S. government proposals and for assessing the propositions of other countries within the Convention.

There are also significant advances in technologies and methodologies that State can take advantage of to make impactful strides in addressing detection, attribution, and verification gaps both for on-site and off-site verification. On-site verification inherently requires access to a facility for inspection. With access, advances in DNA sequencing and data collection have dramatically reduced the cost of sequencing collection as well as novel modalities for inspection. This has led to sequences that are more accurate and detailed with real-time turnaround for results. Once such data is collected, there is greater baseline data on the use of biotechnology with the expansion of the modern biotechnology industry and scientific domains. This has also led to a greater repository of publicly available data on hazardous biological agents through numerous private and public investments such as the Intelligence Advanced Research Projects Activity's (IARPA's) programs FELIX and FunGCAT, which are instrumental in developing next-generation computational and bioinformatics tools to "improve DNA sequence screening, augment biodefense capabilities through the characterization of threat based on function, and to advance our understanding of the relative risks posed by unknown nucleic acid sequences."[213]

The combination of advances in technologies for the inspection of biological agents and a rapidly-expanding body of public and private biological data creates the right conditions for taking advantage of modern big data analysis and high-power computing. In one example, the artificial intelligence company DeepMind recently publicly released the direct sequence to 3D protein structure prediction algorithm AlphaFold[214] along with structural predictions of every known protein in the human proteome.[215] The combination of structural and functional predictions of a sequence in the geopolitical context of where a sample was collected can provide inspectors with a much faster understanding of the biological nature of a sequence of concern.

With the growing dependence on commercial DNA synthesis companies, there are emerging modalities to enhance off-site verification—an approach that the BWC has explored by building relationships with life sciences stakeholders, including the international commercial industry.[216] While many commercial synthesis companies already screen both customers and the sequences being ordered for signs of risks, there is additional opportunity for multilateral cooperation to strengthen these screening methods. A combination of enhanced cooperation and advances in modern computing can provide additional context for sequences of concern.[217]

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212 Within the BWC context, the State Department has an IC bureau known as the Bureau of Intelligence and Research (INR) whose primary mission "is to harness intelligence to serve U.S. diplomacy." See the U.S. State Department - Bureau of Intelligence and Research, "Intelligence and Research (INR)."

213 See Intelligence Advanced Research Projects Activity, "Finding Engineered Linked Indicators," 2021 and "Functional Genomics and Computational Assessment of Threats," 2021.

214 Demis Hassabis, "Putting the Power of AlphaFold Into the World's Hands," *DeepMind*, 2021.

215 "AlphaFold Protein Structure Database," *DeepMind,* 2021.

216 Georgi Avramchev, "Introducing Biosafety and Biosecurity," in *Improving Implementation of the Biological Weapons Convention: The 2007 - 2010 Intersessional Process,* edited by Piers Millett (Geneva, Switzerland: United Nations Publications, 2011): pp. 67 - 72.

217 Piers Millet, Tessa Alexanian, Evan Appleton, James Diggans, Michael Montague, and Alexander J. Titus, "Feasibility of Onsite Verification," *Untitled Book*, forthcoming 2021-2022. See also "International Gene Synthesis Consortium: Where Gene Synthesis and Biosecurity Align," International Gene Synthesis Consortium, 2020; U.S. Department of Health and Human Services, Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA, 2012; and The National Academies - Division of Earth and Life Studies, Sequence-Based Classification of Select Agents (Washington, DC: National Academies Press, 2010).

The Council Chamber at the Palace of Nations in Geneva where the BWC was negotiated. United States Mission Geneva

In addition, the proliferation of web-based content provides opportunities to leverage big data analysis of academic literature, news, and media—both social and reporting—to identify indicators of concern. Newer tools for screening sequences and online content both can provide information to enhance negotiations and multilateral cooperation. In this context, State should promote the development and deployment of such tools, potentially through new cooperative, multilateral mechanisms like those mentioned above.

ENHANCE MULTILATERALISM VIA TAILORED BIO COOPERATION MECHANISMS

The COVID-19 pandemic has demonstrated the acute need for enhancing multilateral cooperation in addressing biological threats. As one of the earliest United Nations organizations, the World Health Organization is vital but not always optimized to fully address emerging biological risks. As noted above, issues in verification continue to slow progress for the BWC. As such, State should help advance creative mechanisms in this regard that complement, but are not constrained by, existing international structures. As one of this report's co-authors wrote in 2019:

> "[A] significant strength to global governance of WMD has been the rise of ad hoc efforts to bolster the primary treaty systems and accelerate progress toward their goals. Many of these mechanisms have been in multilateral and minilateral formats, welcoming small- to medium-sized groups of countries (and often other actors) to join together in committing resources, driving action, and communicating their political commitment to reducing well-defined WMD risks."[218]

In the coming years, State should work with other nations and nongovernmental entities to advance such mechanisms that complement the Biological Weapons Convention (BWC) and help improve the world's capabilities to address

218 Christine Parthemore, "Weapons of Mass Destruction: The State of Global Governance Amid Rising Threats & Emerging Opportunities," *Council on Strategic Risks*, October 2019: p. 12.

biological threats. In the near term, the International Agency for Biological Safety (IABS) proposed by the President of Kazakhstan to the UN General Assembly in 2020 is one potential target. Though nations wishing to advance the IABS have yet to detail its most likely operations and roles, Kazakhstan has indicated an interest in it becoming a hub for data exchange, aiding countries in responsible governance of their bio economies, and supporting investigative efforts to rapidly understand and address outbreaks.[219]

Additionally, Ambassador Ahmet Üzümcü, former director general of the Organization for the Prohibition of Chemical Weapons (OPCW) and a Senior Advisor to CSR, has proposed that countries unite to establish a new institution that would operate an "epidemic early warning center" and "rapid response teams" that deploy to investigate and characterize the threat when a potentially-serious outbreak emerges.[220] Further, this effort could utilize promising technologies like metagenomic sequencing, which can rapidly and effectively analyze samples for all known pathogens. Metagenomic sequencing would also be promising in addressing novel pathogens, including those from natural sources with future pandemic potential as well as synthesized biological weapons.[221]

Modeled from OPCW functions, this could help confer neutrality on work to understand outbreaks and promote science-led decision making. This proposition may be part of the IABS put forth by Kazakhstan or promoted along separate diplomatic lines.

EXPAND DIPLOMACY AND PROGRAMS FOR PATHOGEN EARLY WARNING

Across the international community, there is a growing movement toward creating a global pathogen early warning system.[222] Such a system would go beyond today's biosurveillance systems, which are fragmented and often do not convey information quickly enough to stop infectious diseases before they become outbreaks or worse. The world has the technologies and tools today to transform this landscape into a global early warning system that can identify disease threats in real time and cover their full spectrum effectively---including pathogens that may be engineered or otherwise intended for use as biological weapons.[223] A global early warning system could advance as a component of the operations center and rapid response concepts noted above, or be developed in ways that ensure collaboration across these initiatives.

As these capabilities are being expanded, it is clear that meeting the vision of a global pathogen early warning system will entail significant diplomacy across all nations. The data-sharing it will require necessitates far greater trust and confidence among nations than the world has today---and may require updates to international law or existing cooperative mechanisms. The diplomatic corps of the United States and other countries will need to ramp up training in infectious diseases, the technologies that can help prevent future pandemics, and other related issues. If it has not yet done so, the White House should lead an interagency planning process to guide U.S. diplomacy for advancing pathogen early warning capacity, complemented by a significant ramp-up in cooperative biological engagement activities to ensure the United States leads the world in providing the needed tools and training.[224]

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219 Government of Kazakhstan, "Concept note on the creation of an International Agency for Biological Safety (IABS)," submitted to the Meeting of Experts on Institutional Strengthening of the Convention, Geneva, September 8, 2021.

220 Please see Ambassador Ahmet Üzümcü, "International Response to Pandemics: Is There a Need for a New International Institution?" *Council on Strategic Risks*, April 2020; and Ambassador Ahmet Üzümcü, "Preparing for the Next Pandemic: A Scenario Exercise," *Council on Strategic Risks,* June 2020.

221 One example of metagenomic sequencing that could be put to use as part of multilateral labs and cooperative mechanisms is an open platform called IDseq, 2021.

222 Bajema, Beaver, and Parthemore, *Toward a Global Pathogen Early Warning System*, 2021.

223 Ibid.

224 Bill Beaver, Christine Parthemore, and Dr. Nikki Teran, "Key U.S. Initiatives for Addressing Biological Threats Part 3: The Biological Threat Reduction Program," Council on Strategic Risks, 2021.

APPOINT A SPECIAL ENVOY AND INCREASE BIORISK EXPERTISE

The Department of State's work on biological issues crosses many offices and functions. Many key roles are coupled with nuclear arms control, chemical security, environmental, and other issues. This holds benefits, but can also limit diplomatic capacity for working on bio issues.

One way to address this gap would be to establish a position akin to similar special positions that the U.S. government has created for transnational issues like climate change. This should be an elevation of the current Coordinator for Global COVID-19 Response and Health Security position and its continuation past the current pandemic, and incorporate lessons from the special envoy office State established in 2014 to curate international cooperation to stop the West Africa Ebola crisis. This special envoy and supporting staff should focus on preventing future pandemics, addressing deliberate and accidental biological threats, and advancing biotechnology cooperation with partners around the world, a remit that is broader than traditional health security roles. This should be a highly-empowered position to lead on the initiatives outlined above---and to promote the United States as the partner of choice in advancing bio economies around the world in ways that respect high biosecurity, safety, and nonproliferation standards. The envoy's office would conduct this work alongside counterparts whose responsibilities overlap as part of broader arms control, threat reduction, and environmental portfolios. This may be done with a specific time horizon, such as five years, followed by a reassessment of the international landscape and national needs.

Further, State should increase the number of biosecurity experts to support both the policy development and implementation aspects of addressing biological threats. These experts could serve three main purposes. First, they could provide much-needed expertise on the intricacies and nuances of addressing biological threats. Second, these experts would be exceptionally helpful toward the formulation, implementation, evaluation, and course-correction of actions taken by State to address biological threats. Finally, these experts can serve as leaders who can highlight and advocate for the importance of addressing biological threats as the security environment changes domestically and internationally.

The effectiveness of international cooperation on biological threats is shaped by whether or not State has willing partners in embassies around the world. In general, biological threats should be widely accepted as a core strategic priority given how dramatically the ongoing pandemic has affected the world. Yet staffing and competing priorities may interfere with advancing work to address biological threats.

Foreign service officer capacity has declined precipitously for these and other science, technology, and environmental roles---by one assessment, a decline of more than ⅔ to just 50 such embassy positions from 2004 to 2013.[225] Second, embassy teams in many countries simply juggle many other issues that will compete for their time, from instability to conflict to the conduct of highest-level negotiations that all require significant diplomatic action.

The increasing complexity and transnational nature of biological threats means diplomats with deep expertise in science and technology matters are more important than ever.[226] Therefore, augmenting diplomatic staff with more experts that have biorisk-specific knowledge and experiences, including in embassies, needs to be prioritized. This expertise, in turn, can improve the U.S. ability to understand how biological threats evolve and succeed in cooperative solutions such as those proposed in this report.

Finally, and perhaps most importantly, State has to find a way to ensure that biological threat prevention remains a high priority, resources are increased to a level commensurate with the scale of the risks, and awareness of biological

225 Justine F. Chen, "Reinstituting the ESTH Cone Within the U.S. Foreign Service," *Journal of Science Policy & Governance* Vol. 7, Issue 1, 2015.

226 "The United States Needs a Modern Foreign Service with Science at the Forefront," *National Science Policy Network*, 2021.

Diplomats and experts at the Biological Weapons Convention Meeting of Experts discussed ways to enhance international cooperation in response to disease outbreaks at an August 15, 2013 side event hosted by the U.S. Delegation to the Conference. Eric Bridiers/United States Mission Geneva.

issues survives after the specter of COVID-19 eventually fades. The Office of Policy Planning at State, whose storied history includes the creation of George Kennan's Long Telegram, researches and creates long-term foreign policy visions and objectives for the department. Recognizing the emerging threats posed by science, the Policy Planning staff should include civil servants with a deep knowledge of scientific issues, not limited to biology, to generate the forward-thinking policy needed to address future threats.

CONCLUSION

The role of the U.S. Department of State is a quintessential one in addressing all manner of risks, threats, and opportunities. As Richard Haass, the President of the Council on Foreign Relations pointed out in an interview in 2017, "we have got to understand that what we do in the world is not only good for the world; it's good for us. It's not a form of philanthropy; it's a form of national security."[227] Through its vast influence in the international community and its engagement in both policy and implementation, State has a wide variety of capabilities to draw from to address biological threats in a way that's both good for the world, and good for the United States.

227 "How a Former Diplomat Makes Sense of 'A World in Disarray'," *PBS News Hour,* 2017.

Ramping up personnel to implement policy changes can take years. Yet the U.S. government has multiple mechanisms for getting those with unique knowledge and skills into the right places more quickly. Moreover, workforce trends of individuals moving across more jobs throughout their careers than used to be common make clear that the United States has a great opportunity to tap talented experts for shorter-term stints serving in specific roles. Some mechanisms that already exist and can be further leveraged against catastrophic biological risks include:

Intergovernmental Personnel Act (IPAs). Through this mechanism, experts can be detailed from nonprofit organizations, universities, and elsewhere to provide specific skills to offices in need.[228] IPAs are commonly used to augment an office's scientific and technical experts. It is an ideal mechanism for supplementing the expertise needed across federal agencies to quickly expand the nation's ability to address biological weapons threats.

Liaison Officers, often referred to as LNOs, are assigned across offices that need to collaborate in order to provide knowledge and connections across institutions. The mandate of cross-agency coordination outlined in this report indicates a need for using LNOs consistently. For example, the Centers for Disease Control and Prevention at times provided a liaison officer to the Department of Defense's Chemical and Biological Defense Program, which significantly enhanced programs conducted by both agencies.

Fellowships and Term Appointments. The U.S. government has multiple mechanisms that can be used to bring unique personnel and their skills to addressing biological threats. In many cases, fellows can be hired through contractors to serve in a specific department. The Schedule A(r) hiring authority also allows officials to augment their staff with skilled experts for short-term appointments of one to four years. The long-running AAAS Science and Technology Fellowship is another example of programs that consistently bring bio experts into government, where often they continue into extended public service toward addressing biological threats.[229]

Presidential Management Fellows, or PMFs,[230] can be deployed deliberately to both meet a robust vision for addressing catastrophic biological threats and to help build the careers of young experts. Often, PMFs believe they may not have technical expertise required for serving in offices that counter biological threats, and opt for more rotations with regional or general focuses. It is incumbent on key leaders in offices that address biological threats to reach out to PMFs (and those in charge of placements for these individuals) to recruit them, get them excited about addressing biological threats, and explain how it will enhance their careers. Leaders in addressing biological threats should also seek to recruit Presidential Innovation Fellows to help advance their missions.

228 U.S. Office of Personnel Management, "Policy, Data, Oversight - Hiring Information," 2020.

229 "Host a Fellow: Executive Branch - Science and Technology Fellows," *American Association for the Advancement of Science*, 2021.

230 U.S. Office of Personnel Management - The Presidential Management Fellows Program, "The Opportunity - PMF as a Pathway," 2018.

BUILDING AN INTERAGENCY NETWORK OF CHIEF BIOTECHNOLOGY OFFICERS

Effective development and use of biotechnology is critical to biodefense, deterrence, and pandemic prevention. This makes it necessary for DoD and other agency leadership to stay up to date on relevant technologies and how they can best be leveraged.

To provide this kind of guidance and technical expertise, in 2019 the DoD Office of the Under Secretary of Defense for Research & Engineering created the position of Assistant Director of Biotechnology --- a position now called the Principal Director for Biotechnology. This position leads biotechnology policy and modernization for the DoD, and advises the department on how biotechnology can be used to deter or defend against attacks from adversaries.[231] A particularly important function of this position is to unite the science community and the defense community—ensuring communication is clear, effective, and productive.[232] The people holding this role have unique power to bring about progress, given their close communication with the Under Secretary.

Alexander Titus, who served as the inaugural Assistant Director of Biotechnology, spoke to the importance of this role in a CSR podcast on November 1, 2021:

> "100% of my job was communications. It was being a bridge between the brilliant scientists doing amazing things and the people who care about what we can do with the technology. That translation and that communication is hard. I would hope that the department would have more and more of those translators who can bridge that gap between what it means operationally and what it means scientifically, because I think that goes a long way to demystifying these emerging technologies."[233]

Across the key U.S. agencies discussed in this handbook, each should create a Chief Biotechnology Officer position modeled on this DoD analogue. Developing a network of biotechnology advisors would help ensure that each agency's leadership has a strong grasp on where to place investments in biotech, how to implement emerging technologies, and how to form partnerships with the private sector for optimal success. This would also make it clear with whom across each agency these officers can collaborate and share information to best drive toward the nation's goals in addressing biological threats.

These Chief Biotechnology Officers can contribute a robust understanding of the state of science and how industry works in specific sub-fields, which would facilitate collaboration with innovative companies. Granting these biotechnology advisors access to agency leadership, including assistant secretaries and under secretaries, is especially important to allow their expertise to be fully utilized and their advice to be implemented via programs and budget decisions.

231 John Cumbers, "'With Great Power Comes Great Responsibility' — Meet Alexander Titus The Department Of Defense's Head Of Biotechnology," *Forbes*, 2019.

232 Christine Parthemore, Andy Weber, and Alexander Titus, "Leveraging Biotechnology for Defense with Alexander Titus," *On the Verge*, 2021.

233 Ibid.

Department of Energy Headquarters Sign and Building. Department of Energy.

THE U.S. DEPARTMENT OF ENERGY'S NATIONAL LABORATORIES[234]

Despite significant difficulties in COVID-19 responses, the pandemic has also highlighted the incredible strides gained in modern biotechnology to address biological risks.[235] Indeed, modern biological sciences are a key strategic national asset. The National Laboratories of the U.S. Department of Energy (DOE) have long played important roles in this field and are well-positioned to enhance their work in countering biological threats in the years ahead.

234 Much of the text in this section is drawn directly from Chris Fall, Yong-Bee Lim and Christine Parthemore, "Key U.S. Initiatives for Addressing Biological Threats Part 2: The U.S. Department of Energy National Laboratories," Council on Strategic Risks, June 22, 2021.

235 Christine Parthemore, Anup Singh, and Andrew Weber, *Critical Steps in Preventing Future Pandemics: Early Lessons from the COVID-19 Crisis for Addressing Natural and Deliberate Biological Threats*, The Council on Strategic Risks, 2020.

The DOE has a long history in developing and advancing basic science and technologies for national security and economic advancement. The department has unique capabilities and talent, including leading experts in the fundamental sciences, and cutting-edge tools and infrastructure that public and private partners can leverage to facilitate both discovery and innovation.

The DOE has also mobilized its National Laboratories (the Labs) to respond to a number of significant national and international crises, including the COVID-19 pandemic. Their contributions include genomics and understanding structural biology of the virus, complex epidemiological modeling of disease spread, improved testing, and addressing supply bottlenecks for critical items such as masks, parts for ventilator systems, and consumables for testing kits.[236]

The Labs are the DOE's stewards for the nation's major scientific facilities such as x-ray light sources, neutron sources, supercomputers, cryo-electron microscope equipment, and other infrastructure that is critical for advancing biology and that is used by academia and industry (such as pharmaceutical companies) alike.[237] The Labs also have substantial genomic sequencing and analysis capabilities derived from the Human Genome Project which are now used primarily for the analysis of plants, microorganisms, and other components of environmental biology.[238]

Despite these achievements, DOE's assets and accomplishments in the biological domain are not yet widely recognized. This chapter briefly reflects on several issues that have contributed to this, and presents a strategic shift that DOE should undertake for the National Laboratories along with several tactical policy updates that will support this shift. Together, these recommendations can help position the United States to maximize the assets the National Laboratories hold for addressing catastrophic biological threats.

INTRODUCTION

Two central thrusts will help drive effective support for U.S. biosecurity in the future. First, the Labs need to build the talent, laboratory infrastructure, and programmatic support necessary to lead in the current frontier of biology---a frontier now led by academia and private companies and geared toward the engineering of novel pathways, functions, and even whole organisms. Second, they need to overcome artificial limits and perceptions that prevent the National Labs from leveraging their unique capabilities and their expertise in science at scale.

It is time to address these issues so DOE can function as a key component of national efforts to prevent future pandemics, deny deliberate biological threats of their potential for mass effect, maintain U.S. leadership in biotechnology, and apply the fruits of scientific competition and modern biological sciences toward the future of mankind and the health of the planet.

To do so, the U.S. government should launch a strategic shift that positions the Labs to be at the forefront of research in engineering biology, with a goal of strengthening the nation's biosecurity while also leveraging the Labs' capabilities for the bioeconomy. Engineering biology is key to core energy and environmental missions of the DOE such as bio-derived fuels and U.S. competitiveness in the products and processes of the bioeconomy. Engineering biology is also a critical capability for national security. Uniquely in the United States, the Labs are capable of basic and applied

236 Department of Energy, Office of Science, "National Virtual Biotechnology Laboratory (NVBL)."

237 Department of Energy, *The State of the DOE National Laboratories*, 2020: pp. 19 - 23.

238 Department of Energy, Office of Science, "Genomics."

research, innovation and technology transfer, and participation in sensitive national security missions often requiring very specialized and restricted facilities. It is critical that the United States have first-rate talent and infrastructure within the federal system to participate in the new and profoundly important field of engineering biology, not least in order to prepare for and to respond to biological threats. The DOE Labs are the appropriate place for this capability.

A number of strategic and tactical policy and programmatic measures would support this shift. Specifically, the U.S. government should:

- Implement program and facility funding for engineering biology, with a special focus on biosecurity, to make the Labs leaders in this critical area of biotechnology and facilitate related academic and private sector partnerships. This should include a focused effort to develop and disseminate platform technologies for engineering biology across the Labs and with interagency and private sector partners.

- More clearly define the mission, roles, and responsibilities of DOE and the Labs as a part of the national biosecurity framework, as well as provide intramural and extramural programmatic support and authorities for the DOE biosecurity mission. The Labs have unique expertise concerning biological threats that are critical for human biological research related to biosecurity.

- Launch a Biosecurity Reserve Corps to better allow nongovernmental experts to surge into cooperation with the Labs when potentially-significant biological threats emerge.

- Re-establish the Chemical and Biological Nonproliferation Program (CBNP) within the DOE. CBNP was a vital program established in 1997 that developed a wide variety of capabilities, technologies, and demonstrations to address biological and chemical threats.[239]

- Integrate the Labs better into the wider bioeconomy. This includes developing a permanent coordination framework that simplifies the interface for tapping into the resources and capabilities of the Labs, incentivizes the Labs to coordinate their activities and enhance cooperation in biotechnology, and facilitates public-private partnerships and technology transition particularly with leading private sector centers of biotechnology.

The next sections provide a short overview of the DOE Labs, as well as a short overview of capabilities and characteristics that enable them to prove that they are a critical element in addressing historic and ongoing biological threats. We then elaborate on the specific recommendations above, reinforced by examples of ways to enhance and better integrate the DOE Labs into the biological threat response space. Finally, this section will end with a set of critical points on implementation. With these steps, DOE can make significant progress in tapping the full potential of the Labs in effectively addressing biological threats and preventing future pandemics.

239 Department of Defense, Department of Justice, Department of Energy, and the Technical Support Working Group, *Integrated Chemical and Biological Defense Research, Development, and Acquisition Plan: Chemical & Biological Point Detection Decontamination Information Systems*, 2003: pp. 7 - 82.

Pacific Northwest National Laboratory Scientist Becky Hess uses techniques such as DNA sequencing to identify the origin and makeup of biological material. Andrea Starr/Pacific Northwest National Laboratory

NATIONAL LABS: A BRIEF OVERVIEW

The DOE Labs have a rich history that has primed them to take a more prominent role in addressing biological risks. The Labs have expanded significantly in number, missions, and scope since their emergence in World War II. Compared to the goal of designing and producing the world's first nuclear weapons in the 1930s and 1940s, the Labs now face myriad challenges ranging from the need for innovation in energy and materials to the detection and attribution of chemical, biological, radiological, and nuclear threats, including biological threats from natural, accidental, and intentional sources.[240]

Cutting-edge work at the intersection of science and national security is conducted across the agency's network of 17 Labs. Their work includes energy innovation, science discovery, nuclear security and weapons activities, and environmental cleanup. They also contribute significantly to research and development in the basic and applied life sciences through initiatives such as the Human Genome Project in the 1990s, the Biological Aerosol Sentry and Information System (BASIS) in the 2000s, and biological detection platforms like the Lawrence Livermore Microbial Detection Array in the 2010s.[241]

The Labs vary in capabilities, structure, and aims, as well as in how they support technical efforts across the interagency and in public-private partnerships. Some Labs are considered energy technology laboratories. Others are considered

240 The Commission to Review the Effectiveness of the National Energy Laboratories, *Securing America's Future: Realizing the Potential of the Department of Energy's National Laboratories*, Volume 1: Executive Report, 2015: pp. 5 - 15.

241 For examples, see "What is the Human Genome Project," *National Human Genome Research Institute*, 2018; Department of Energy, Lawrence Livermore National Laboratory, "Lab's Work Provides BASIS for Biodetection," by Stephen Wampler, September 7, 2011; and Department of Energy, Lawrence Livermore National Laboratory, "Microbial Detection Array," 2021.

multipurpose science laboratories, with unique research programs, core capabilities, and facilities that enable cutting-edge scientific research and outcomes. Yet others are considered single-program science laboratories, which focus exclusively on basic science. Finally, multipurpose security laboratories are fundamental to addressing nuclear, chemical, biological, and radiological threats through cutting-edge science and engineering in both the open and classified domains.

Further, the Labs house exceptional multidisciplinary expertise. In basic science research alone, experts from the Labs have discovered 22 of the 118 elements on the periodic table and received 118 Nobel Prizes.[242] This in-house expertise has enabled innovation across the spectrum of science, technology, engineering, and mathematics disciplines.[243]

The Labs are also known for their cutting-edge facilities that house some of the world's most unique and advanced scientific instruments and tools. A well-known asset housed in the Labs lies in their hosting some of the world's fastest supercomputers---extremely powerful computers whose speed and capacity enable researchers to model and analyze complex biological, chemical, nuclear, novel materials, climate, and energy-related systems.[244] These supercomputers are also integral to ensuring the safety, security, and effectiveness of the U.S. nuclear stockpile and contribute to U.S. support of the Nuclear Test Ban Treaty. This, alongside other technologies and resources like large-scale particle accelerators, lasers, nanoscience and genomic centers, x-ray light sources, and neutron sources play a significant role in Labs and their unique abilities.[245]

CAPABILITIES OF THE NATIONAL LABS FOR ADDRESSING BIOLOGICAL THREATS

Across the 17 DOE National Laboratories, there are wide-ranging assets for contributing to national efforts to address biological threats. These include world-class facilities, experts across a range of disciplines, and strong relationships with other government agencies, academia, and private companies.[246] These capacities are most visible at times when biological threats emerge and affect the United States and the world.

The United States was fortunate to have the Labs' expertise as the 2001 anthrax attacks unfolded following the September 11 terrorist strikes. Sometimes referred to as the Amerithrax incident, this event caused 22 infections and 5 deaths, over a billion dollars spent to decontaminate attack sites, and immense psychological and political impact in the United States and abroad due to the spread of anthrax spores via letters sent through the U.S. Postal Service.[247] As Amerithrax transpired, the U.S. government put together a team of experts with diverse backgrounds in biomedicine, bioinformatics, forensics, engineering, and biodetection and analysis from Lawrence Livermore National Laboratory (LLNL) and Los Alamos National Laboratory (LANL) to set up a field-ready system of detection and analysis technologies for pathogens in the nation's capital. This resulted in the implementation of the Biological Aerosol Sentry and Information System (BASIS) - a system that reduced the time for detecting a biological agent's release from days or weeks to less than a 24-hour period.[248]

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242 The exceptional number of Nobel Prize winnings is not just a historical footnote - for example, from 2015 - 2020, national laboratory experts were the recipients of 38 Nobel Prizes. See U.S. Department of Energy, *America's National Laboratory System: A Powerhouse of Science, Engineering, and Technology,* 2017: pp. 1 - 36; *The State of the DOE National Laboratories*, 2020: p. 16; and Department of Homeland Security, Science and Technology Division, *DHS and DOE National Laboratories: An Enduring Partnership*, 2021: pp. 1 - 2.

243 *The State of the DOE National Laboratories (2020)*: p. 17.

244 National Nuclear Security Administration, "NNSA Supercomputers Recognized Worldwide for Speed and Performance," 2020.

245 For examples, see The State of the DOE National Laboratories. 2020: p. 10 and Department of Energy, Office of Science, "NVBL Projects," 2020.

246 Department of Energy, *The State of the DOE National Laboratories,* 2020: pp. 7 - 9.

247 United States Department of Justice, *Amerithrax Investigative Summary*, 2010: pp. 1- 16.

248 Wampler, "Lab's Work Provides BASIS for Biodetection."

Further, facilities and capabilities such as exquisite imaging and computational biology that the Labs possess allow scientists to innovate ways of characterizing, analyzing, and monitoring biological specimens---critical steps in identifying both promising biological specimen candidates for novel applications and potential biological threats. An important element of the Amerithrax investigation was determining the age of the anthrax spores. Knowing this key piece of information would provide a rough idea of when the anthrax used in the attacks was produced. Fortunately, assets like the Center for Accelerator Mass Spectrometry at LLNL provide researchers with access to state-of-the-art instruments and analytical techniques. This Center developed critical advances in forensic science and its applications.[249] These applications, such as carbon dating methods for biological samples, were pivotal in providing preliminary data on the age of anthrax spore samples, the essential information the investigation required to generate a temporal window of when the material was produced.[250]

Finally, the Labs occupy a unique space at the nexus of science mobilization and national security. This distinct vantage point allows the Labs to both lead and support in the characterization and development of technical solutions. This was particularly visible during the COVID-19 pandemic when DOE set up a virtual laboratory to mobilize Lab facilities and experts at a single point of contact.[251] Funded through the CARES Act of 2019, the National Virtual Biotechnology Laboratory (NVBL) brought the best of core Lab capabilities online to function as one integrated team across the entire complex. The NVBL has provided significant benefits during COVID-19 through 1) developing complex epidemiological modeling leveraging the world's fastest supercomputers; 2) leveraging advanced materials and additive manufacturing capabilities to help address supply chain issues for critical medical supplies, equipment, and personal protective gear; 3) assisting in molecular design through artificial intelligence, materials characterization, and nanoscience research to produce promising therapeutics for COVID-19; 4) gathering and using data to better understand the emergence, circulation, and resurgence of COVID-19 and future pathogenic microbes; and 5) providing access to supercomputer-driven simulation and model capabilities to interested researchers working toward ending the pandemic.[252] While less of a concern in the COVID-19 response, the Labs also are uniquely situated to work across the government and private sectors, with facilities, scientists and staff capable of operating in both the classified and unclassified domains.

This blend of expertise, facility capabilities, and innovation hubs has allowed the Labs to catalyze new testing capabilities, identify novel targets for medical therapeutics, generate real-time and predictive epidemiological models of COVID-19 spread, and shatter bottlenecks in the supply chain process through materials science and additive manufacturing.[253] With a few new policies and programs, the Labs can build on these contributions and maximize their capabilities for future efforts.

RECOMMENDATIONS

The Labs have contributed to the safety, security, and prosperity of the United States, its allies, and the world from past to present, and there is no need for this trend to cease. In fact, there are ways to more fully leverage the unique capabilities of the Labs to meet present and future challenges in the biothreat space. While this will take time, the following ideas can be put in motion immediately.

249 Department of Energy, Lawrence Livermore National Laboratory, "A Brief History of CAMS," 2020.

250 National Research Council, *Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Anthrax Letters* (Washington, DC: National Academies Press, 2011): pp. 73 - 75.

251 David Kramer, "DOE Launches 'Virtual' National Lab to Counter Coronavirus," *Physics Today*, 2020.

252 United States Department of Energy, "NVBL Projects."

253 Philip Rossetti, "Publicly Funded National Labs Important to U.S. Innovation," *American Action Forum*, 2018.

MAKE DOE AND THE LABS LEADERS IN ENGINEERING BIOLOGY

One of the most profound developments of the 21st Century will be the evolution that is already taking place in bioeconomies around the world: the convergence of genomics, synthetic biology, engineering, and computation, referred to as engineering biology. In the United States, companies and academics are at the forefront of driving the basic and applied research advancements that contribute to engineering biology. Though the U.S. government has begun to shift toward a more proactive position in the field, this transition remains somewhat limited to biological threat response: monitoring and defending against biological threats and responding to infectious disease threats after they emerge.

The optimal strategy for both U.S. security and economic interests is to ensure the nation remains at the cutting edge of the life sciences consistently over the coming decades, and equally across the public and private sectors. This transition is necessary to move from reactive to proactive efforts to address biological threats. Given their unique expertise, capabilities, and innovative potential, it is clear the DOE Labs should play a key role in this strategic shift by augmenting its existing capabilities to become a leader in engineering biology.

Many of the necessary ingredients for this already reside in the Labs: expertise in synthetic biology, artificial intelligence and machine learning, materials sciences, computational sciences, and the identification, detection, classification, and characterization of biological specimens. The facilities in these spaces allow experts to collaborate and do everything from field testing new tools to conducting cutting edge basic research that opens the door for new applications in the life sciences. The Labs also serve as hubs of innovation that transfer technologies between the public and private sectors---a connection that is not nearly as established in other parts of the interagency. What is missing is the identification of engineering biology as a DOE priority for the bioeconomy and biosecurity, and a focused effort to fill gaps in capabilities and to recruit world-class talent specializing in integrating the convergent fields that contribute to engineering biology.

The sequencing laboratory of the DOE Joint Genome Institute (JGI) on the first floor of the Integrative Genomics Building at Berkeley Lab. Left to right: Hope Hundley (loading a Oxford Nanopore PromethION), Laura Sandor (loading a Pacific Biosciences Sequel II), and Jenifer Johnson (loading an Illumina NovaSeq).
THOR SWIFT/THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, LAWRENCE BERKELEY NATIONAL LABORATORY

The Labs should host world-class infrastructure for cutting-edge engineering biology, and DOE should provide the intramural and extramural programmatic support necessary for the Labs to lead and to create meaningful partnerships with academia and the private sector. Leadership in engineering biology is more critical than ever in a 21st century that is rife with security threats. As the Labs are more fully leveraged to cement U.S. primacy in the life sciences, these spaces will produce a whole host of field-ready capabilities in areas of biological detection, attribution, and the accelerated research, development, and manufacture of rapid medical countermeasures. As these capabilities are brought online in the coming years, enhanced proficiencies in these critical areas can have great benefits toward pandemic prevention and deterring and dissuading actors from biological weapons activities.

CLARIFY AUTHORITIES AND INTERAGENCY DEPENDENCIES FOR THE DOE BIOSECURITY MISSION

DOE has not always had a recognized seat at the table in the biosecurity mission space. Fuller and clearer authorities would better empower DOE to operate in the biological space and to dedicate appropriate resources to this mission. As one example of the lack of clarity, DOE was not originally listed as a primary member of the cabinet-level Biodefense Steering Committee (BSC) established in the 2018 National Security Presidential Memorandum (NSPM) 14 for "monitoring and coordinating the implementation of the [National Biodefense] Strategy."[254] The Labs have clear utility in addressing all five goals in the National Biodefense Strategy, and the DOE participated in the drafting of both the Strategy and the Implementation Plan.[255] Recognizing the important role of DOE and the Labs in biosecurity, the Secretary of Health and Human Services (HHS) subsequently invited the Secretary of Energy to join the BSC as a permanent primary member, and this was finalized in a revision to the charter in September 2020 during the COVID-19 crisis. While operational agencies such as DOE and HHS work well together and understand their respective capabilities and roles, there remains confusion in Congress, in the Office of Management and Budget, and in policy organizations such as the Office of Science and Technology Policy and the National Security Council regarding the appropriateness of full DOE participation in biosecurity matters.

A second concern is a lack of clarity and consistency in terms of programmatic support for the Labs from other biosecurity mission agencies. For example, following the establishment of the Department of Homeland Security Science and Technology Directorate (DHS S&T) in 2003, the Labs were sponsored to serve at DHS S&T to help develop and manage research and development for the directorate. These efforts included highly salient areas in addressing biological threats like the research and development of assays, detection systems, bioinformatics systems, and operational support. One of the most visible, and most-discussed, technologies associated with this merger was the BioWatch system---an early-warning detection system for certain pathogens that may be released in the environment for deliberate, offensive purposes.[256] However, the expertise housed within the Labs was sidelined as DHS stood up its own initiatives and operations. Experts from the Labs were phased out in key ways, including denial of access to S&T planning meetings on projects that Labs had helped set up.[257] It is impossible for the Labs to plan for necessary facilities, resources, and personnel that other agencies might need to leverage for biosecurity without predictable, long-term support and relationships.

Clearly defined authorities would help ensure that the unique expertise and capabilities of the Labs are effectively put to work in biosecurity matters across the interagency. A consistent understanding of responsibilities within the interagency biosecurity space is necessary to better leverage the Labs for biosecurity work and also to facilitate enduring partnerships with academia and the private sector in engineering biology.

254 The White House, "Presidential Memorandum on the Support for National Biodefense," 2018.

255 The White House, *National Biodefense Strategy*, 2018: pp. 6 - 7.

256 A.M. Waters, *LLNL and DHS Science and Technology Directorate - Historical Relationship*, 2018: pp. 4 - 7.

257 Ibid.

CREATE A BIOSECURITY RESERVE CORPS

The Executive Branch and Congress should create a system to strengthen the nation's ability to leverage top talent across public and private sectors. One such system could be a Biosecurity Reserve Corps. Somewhat akin to the National Guard, nongovernmental experts could sign on for a period of service via the National Labs. This could entail a minimal annual time commitment (for example, 5 days per year) spent networking with Lab counterparts and collaborating with them, and allow Corps members to be pre-credentialed and cleared in order to surge into national service if their help is required to urgently address an emerging biological threat.

This system would be advantageous in three ways compared to the status quo. First, lowering the barriers for DOE experts to build and maintain formal relationships with private industry and academics is necessary to keep the United States on the cutting edge of the life sciences and the disciplines it affects. Disciplines like synthetic biology show that the life sciences have become de-siloed. As subject areas like engineering, computer science, and data informatics continue to gain greater relevance in the life sciences, it is extremely unlikely that all relevant expertise will be found in one location. Therefore, building the networks now is of vital importance to the U.S. global position in science and technology research and development, as well as providing a regular mechanism for experts across the public and private sectors to trade ideas and to build interpersonal relationships ahead of a crisis.

Second, when biological threats emerge, the nation could build on this Biosecurity Reserve Corps concept and the network it promotes to enable swift action with minimal operational and bureaucratic barriers. During such events, Corps members would already be pre-credentialed to facilitate onsite access to Labs. All necessary paperwork and agreements would be completed before a crisis strikes. Eliminating delay through pre-credentialing Biosecurity Reserve Corps members enables a faster response time to more immediately address a biological threat while minimizing the operational burden in a swiftly-evolving emergency environment.

Finally, the Biosecurity Reserve Corps could allow the Labs to better compete in attracting and retaining the best and the brightest scientific and engineering minds. Some recruitment and retention issues at the Labs derive from common competition with companies that offer high salaries and other perks. Such problems also stem from cultural changes: historically, career models for laboratory staff were usually based on long-term and stable work experiences - it was not uncommon for individuals to have one or two positions for significant stretches of time until retirement. In contrast, current trends indicate that people are comfortable changing job positions more frequently in order to have a wider variety of experiences.[258]

The Biosecurity Reserve Corps can help overcome these challenges, as talented people will not have to choose this lifestyle over public service. This will help the U.S. government tap into the many benefits that can come from experts taking on diverse experiences. To facilitate a strong start to the Corps, more analysis should be done on the incentives and disincentives that influence younger generations as they consider working in government versus other sectors. In addition, this should include an analysis of the rate and implications of retirement in particular areas of the national security enterprise.

RE-ESTABLISH THE CHEMICAL AND BIOLOGICAL NONPROLIFERATION PROGRAM (CBNP)

CBNP was established in 1997 in response to growing concerns about chemical and biological weapons capabilities and their potential use by state and non-state actors. This program was housed in the DOE with a crucial national

258 Trent Northen, Nancy Hagel, Daniel Sinars, Johnny Green, Dawn Wellman, and Daniel T. Schwartz, *Attracting and Retaining Top Scientists and Engineers at U.S. National Laboratories and Universities: Listening to the Next Generation*, 2018: pp. 1 - 6.

security mission: to develop, demonstrate, and deliver technologies that improve domestic defense capabilities against chemical and biological attacks and save lives.[259] The program resulted in a number of innovative solutions to achieve that mission, including detectors and diagnostics for chemical and biological threats.

Eventually, as with many Lab projects with biosecurity implications, CBNP was moved to the newly-established Department of Homeland Security (DHS) in 2003.[260] Again, the transfer of a biosecurity program from the Labs to DHS contributed to the loss of DOE input in significant areas related to addressing biological threats. An analogous program should be reestablished in DOE, especially given the above-noted advantages in applying technological changes to this mission---infrastructure that DHS simply does not have. This work should still be tightly coordinated with interagency counterparts to avoid duplication and best leverage all federal assets, but the Labs need an independent program to ensure that their input and projects are not lost in pursuit of countering biological and chemical threats.

INTEGRATE THE LABS INTO THE WIDER BIOECONOMY ECOSYSTEM

Historically, the Labs have been underleveraged when it comes to public-private partnerships. A contributing factor to this issue is how geographically distant many of the Labs are from metropolitan regions - and, in particular, metropolitan regions hosting significant concentrations of private companies and academic institutions researching and innovating in the life sciences.[261] While this geographic chasm was generated deliberately due to the security-focused and sensitive nature of the Labs' early missions, this severely limits the Labs in building the necessary public-private partnerships to help fulfill some of their vital missions in areas like technology transfer for commercialization.[262]

Therefore, it is essential to develop a permanent coordination framework that facilitates public-private interactions, simplifies the interface for tapping into their resources and capabilities, and incentivizes the Labs to collaborate and build bridges with the private sector. The Labs can take lessons learned from successes such as the NVBL to explore future platforms that are oriented more toward developing and accelerating the bioeconomy and to further engage with geographically-distant private entities, interagency partners, and other stakeholders who also can contribute to the biosecurity mission as needed.

IMPLEMENTATION

Implementing these recommendations will require action in several cross-cutting areas of activity. Steps to facilitate progress include the following.

Enable Full DOE Representation on Bio-Related Matters. Despite their utility in biological research, development, and application across a wide range of sectors, DOE has too often been left out of committees or councils that deal with bio-related matters. The roles of DOE leadership and the Labs in vital biosecurity coordination efforts like the Biodefense Steering Committee and associated working groups need to be clarified, and they should participate

259 U.S. Department of Energy, Defense Nuclear Nonproliferation Office, *Chemical and Biological Nonproliferation Program: FY99 Annual Report,* 2009: pp. 5 - 9.

260 Counterproliferation Program Review Committee, *Report on Activities and Programs for Countering Proliferation and NBC Terrorism*, 2003: pp. 11 - 12.

261 CBRE, "U.S. Life Sciences Report 2020."

262 Scott Andes, Mark Muro, and Matthew Stepp, *Going Local: Connecting the National Labs to their Regions to Maximize Innovation and Growth*, 2014: pp. 5 - 9.

in all future biosecurity strategy documents and convening bodies. DOE personnel should also be present for key interagency decisions and deliberations---for example with bio-related discussions convened by the National Security Council (NSC) and Office of Science and Technology Policy (OSTP).

Implement Biothreat-related Projects that Fully Utilize DOE Labs and their Expertise. Improving on the success of platforms like the NVBL and past research, development and deployment of detection technologies will be key to addressing the next pandemic. Now is the time to build on past programs like CBNP and generate new initiatives that enhance our efficiency at both detecting and understanding pathogens of concern. This is vital to the nation's and the global community's continued health and security.

Improve Communications. For many policymakers and influencers, the public, and even personnel across U.S. government agencies, there is a lack of full appreciation for how deep DOE's capabilities are in terms of reducing biological risks. DOE officials and other stakeholders should develop stronger messaging and outreach strategies as a foundation for improving policies and practices surrounding the Labs.

Rededicate the National Nuclear Security Administration (NNSA) to the biosecurity mission. Though its focus is on nuclear matters, in particular the U.S. nuclear weapons stockpile, those leading the NNSA are key decisionmakers and advisors to the Secretary of Energy (and White House leadership) broadly in matters of national security. Undertaking the strategic shift toward the Labs leading in engineering biology, and other recommendations outlined above, would benefit from the advice and ideas of NNSA leaders---in addition to making sure meeting the full biosecurity potential of the Labs is harmonized with other DOE missions. The CBNP has a natural home within the NNSA and its laboratories.

Leverage the Labs' Systems Thinking. Improving national security requires systems-level thinking and problem-solving for which the Labs are uniquely suited. As the threat space continues to evolve (and defy the boundaries of government programs that too-often compartmentalize solutions), diverse input and expertise are necessary to address a national security space that is becoming increasingly de-siloed and complex. The Labs are historically unique in being managed in ways that encourage the multidisciplinary approaches necessary to countering modern threats.

CONCLUSION

The DOE Labs have been described as the "crown jewels of the nation's research and innovation ecosystem."[263] Their past and current performance in the area of biological threats makes it clear that this phrase is a perfect description for the Labs: spaces where some of the brightest minds in the United States gather and use cutting-edge equipment and facilities to help drive the efforts necessary for the nation's health, security, and prosperity. By further leveraging and empowering the National Labs, the United States can continue to reap the benefits of these critical assets, and be better prepared for the complex risks of the 21st century.

263 Department of Energy, "Impact of DOE's National Labs Felt Both Locally and Internationally," 2016.

Department of Homeland Security building and sign. Government Accountability Office.

THE U.S. DEPARTMENT OF HOMELAND SECURITY

Since its founding in 2002, DHS has been an integral part of how the United States addresses deliberate biological threats. Two main organizations within DHS contribute significantly toward developing and coordinating the actions prescribed by national strategies for countering terrorism. One is the Countering Weapons of Mass Destruction (CWMD) Office, which focuses on anticipating and assessing such threats in the United States while also carrying out operations to detect and disrupt them.[264] The second is the Science and Technology (S&T) Directorate, which conducts basic and applied research, development, testing, and evaluation activities to address a broad range of threats, including biological ones.[265]

264 Department of Homeland Security, "Countering Weapons of Mass Destruction Office," 2021.

265 Department of Homeland Security, "About S&T," 2021.

Additionally, while many other agencies have taken lead roles in addressing the emergence, spread, and consequences of COVID-19, the U.S. Department of Homeland Security (DHS) has been involved through independent and interagency collaborations. To address the unique challenges of air travel safety and security during a global pandemic, one of the most visible efforts DHS has undertaken is to modify its practices and provide additional resources and information to air travelers.[266] DHS also engages in technical efforts to characterize and address the threats associated with COVID-19, including the development of an online calculator that helps predict the decay rate of SARS-CoV-2 given factors like the ultraviolet index, ambient temperature, and relative humidity.[267]

This chapter focuses on the roles, capabilities, and activities of DHS-CWMD and DHS-S&T as they relate to the vision set forth in this handbook. It will begin with a brief history of DHS and these offices. It then provides recommendations on how DHS components can be improved upon to address the evolving landscape of biothreats that the United States faces. Finally, this chapter concludes with some recommendations on implementation and future steps.

BACKGROUND

The events surrounding September 11, 2001, left an indelible mark on the United States and its future trajectory. A month later, America had to deal with the 2001 anthrax attacks (Amerithrax), which involved a terrorist mailing 5 letters that contained anthrax spores to prominent senators and several media outlets.[268] Unfortunately, as the spores became aerosolized through the mailing process, mailing facilities and recipients were exposed and contaminated, resulting in 5 deaths and 17 infected and costing nearly a combined $1 billion in decontamination efforts.[269]

The Homeland Security Act of 2002 mandated the formation of DHS.[270] The purpose of this new cabinet-level agency was to address the perceived growing threat of acts of terrorism, including bioterrorism, against the United States on domestic soil.[271] Organizationally, DHS was formed through the incorporation of 22 government agencies, whose responsibilities included customs and border protection, emergency preparedness and response, intelligence analysis and infrastructure protection, science and technology development, narcotics control, and coordination involving the federal, state, local, foreign governments and private sector.[272]

Just as threats to the United States have evolved, so has DHS. The agency has focused on independent and collaborative efforts to enhance efficacy in mission areas such as addressing counterterrorism and homeland security threats, securing cyberspace and critical infrastructure, strengthening U.S. preparedness and resilience, securing U.S. borders and approaches, and better integrating DHS expertise and capabilities across the interagency.[273] These efforts have historically involved

266 For examples, see Department of Homeland Security, "DHS Responds: Coronavirus (COVID-19)," 2021 and Department of Homeland Security, U.S. Customs and Border Protection, "CBP COVID-19 Updates and Announcements," 2021.

267 "Department of Homeland Security, Science and Technology Directorate, "Estimated Surface Decay of SARS-CoV-2 (Virus that Causes COVID-19)," 2021.

268 Glenn Cross, "Death in the Air: Revisiting the 2001 Anthrax Mailings and the Amerithrax Investigation," *War on the Rocks*, 2019.

269 There are varying ranges depending on the analyses and scope related to the Amerithrax clean-up. Please see Government Accountability Office, *Capitol Hill Anthrax Incident - EPA's Cleanup Was Successful; Opportunities Exist to Enhance Contract Oversight*, 2003; Randolph E. Schmid, "Anthrax Cleanup Nearing End," *Associated Press,* June 14, 2002; National Academies of Sciences, *Reopening Public Facilities After a Biological Attack: A Decision Making Framework,* 2005: pp. 56 - 72; and Federal Bureau of Investigation, *Amerithrax Investigative Summary*, 2010.

270 Charles Perrow, "The Disaster after 9/11: The Department of Homeland Security and the Intelligence Reorganization," *Homeland Security Affairs* Vol. 11, Issue 1, 2006: Article 3.

271 Harold C. Relyea and Henry B. Hogue, *CRS Report for Congress - Department of Homeland Security Reorganization: The 2SR Initiative*, 2005.

272 Raphael Perl, "The Department of Homeland Security: Background and Challenges," in the National Academies of Sciences' Terrorism: Reducing Vulnerabilities and Improving Responses: U.S.-Russian Workshop Proceedings, 2004.

273 Department of Homeland Security "Mission," 2021.

actions such as enhancing information-sharing with DHS partners, increasing preparedness exercises and measures for catastrophic events, and regular reviews from both internal and external stakeholders to maximize mission performance.[274]

To fulfill its mission of developing and coordinating the actions prescribed by U.S. national strategies, DHS leverages its capabilities and assets to take a four-pillar approach to addressing natural and anthropogenic biological threats:[275]

- **Threat Awareness:** DHS Science and Technology (S&T) has programs that build the infrastructure to acquire and share information streams and tools across experts and members of the interagency. This infrastructure catalyzes how DHS and other agencies assess and prioritize biological risks and threats.[276]
- **Prevention and Protection:** DHS S&T also works with partners in academia to address the changing nature and emerging challenges of biological threats. One partnership is through a network of universities known as Centers of Excellence (COEs). Recently, DHS and COEs have been working on using new tools like machine learning to develop more robust and complex risk models and matrices for responding to biological threats.[277]
- **Surveillance and Detection:** DHS has also leveraged technological platforms as a step towards accurate and effective detection of biological threats. DHS is commonly known for the BioWatch Program - a program intended to detect biological agents and provide early warning in the event of a biological attack.[278]
- **Response and Recovery:** DHS has leveraged interagency biodefense exercises, which include state and local officials, to train and generate lessons learned in preparation for future bioevent responses. Further, DHS has developed bioforensics capabilities that help support the identification of bioevent perpetrators to stymie future attacks.[279]

The following section provides brief descriptions of advances and issues in each of these areas, along with recommendations for continuing to build on DHS's work in addressing biological threats.

DHS AND BIOLOGICAL THREATS

Since its inception, DHS has considered biological events from natural and deliberate sources to be increasing in likelihood and potentially in scale of devastation. A significant biological event could result in millions of casualties due to the unique propagating nature of many pathogens. These concerns are exacerbated in part by the evolving character of terrorism within the United States and around the world. In addition, the increased accessibility to life

274 For example, see Harold Relyea, *CRS Report for Congress - Homeland Security: Department Organization and Management - Implementation Phase*, 2004; Government Accountability Office, *Report to Congressional Requesters - Countering Violent Extremism: DHS Can Further Enhance its Strategic Planning and Data Governance Efforts*, 2021; and Government Accountability Office, *Report to Congressional Committees - Biodefense: After-Action Findings and COVID-19 Response Revealed Opportunities to Strengthen Preparedness*, 2021.

275 Office of Homeland Security, *National Strategy for Homeland Security*, July, 2002.

276 Department of Homeland Security, Science and Technology Directorate, "CBD Focus Areas - Threat Awareness," 2021.

277 Amelia Brust, "Centers of Excellence Help DHS Combat Bio Threats, Domestic Terrorism," *Federal News Network*, 2021.

278 Department of Homeland Security, *Office of the Inspector General Report: Biological Threat Detection and Response Challenges Remain for BioWatch (REDACTED)*, 2021.

279 Department of Homeland Security, "Biological Security," 2012.

sciences knowledge, equipment, and materials are also driving concerns that complex bioterrorism attacks are within the reach of terrorist organizations and lone wolves.[280]

The importance of the DHS mission in addressing biological threats is highlighted in two past Homeland Security Presidential Directives (HSPDs). In 2004, the White House issued HSPD-10, a directive that tasked DHS with conducting biennial biological threat assessments due to how "biological weapons could cause catastrophic harm" and "preventing and controlling future biological weapons threats will be even more challenging" given advances in biotechnology and the life sciences.[281] In 2007, the White House issued HSPD-18, which expanded the aperture of DHS to implement an integrated threat assessment for chemical, biological, radiological, and nuclear (CBRN) threats.[282]

DHS currently frames its approach to addressing biological threats through the same framework provided in the 2018 National Biodefense Strategy, a document that provides a vision and an implementation plan for "effectively preventing, preparing for, responding to, recovering from, and mitigating risks from natural, accidental, or deliberate biological threats."[283] This framework considers DHS's contributions in the categories of threat awareness, prevention and protection, surveillance and detection, and response and recovery.[284]

THREAT AWARENESS - OPTIMIZING DATA SHARING AND USE

DHS relies on information acquisition, analysis, and distribution to assess the current state of biological threats against the United States. DHS acquires information from numerous sources, including internal sources like pathogen threat characterization done at the National Biodefense Analysis and Countermeasures Center (NBACC), as well as information from public health, intelligence, and law enforcement agencies.[285] This information is then integrated in centers like DHS's National Biosurveillance Integration Center (NBIC).[286] As data is acquired and integrated, it is used in risk assessments such as the DHS Bioterrorism Risk Assessment (BTRA) to help identify and fill knowledge gaps, as well as helping DHS and its collaborators identify potential paths forward to counteract existing and future biological threats.[287] In addition, this information is compiled and housed in repositories such as the Biodefense Knowledge Center (BKC), a collaborative project of DHS and the Department of Energy. Finally, this information, and associated assessments and other products, are distributed from DHS and other federal agencies to state, local, and tribal governments via fusion centers.[288] This threat assessment work can be seen in DHS fusion centers and NBIC, which coordinate the gathering, analysis, and dissemination of salient information across federal agencies, as well as state, local, and tribal governments.

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280 See National Research Council, *Department of Homeland Security Bioterrorism Risk Assessment: A Call for Change*, 2008; Department of Homeland Security, *Quadrennial Homeland Security Review Report: A Strategic Framework for a Secure Homeland*, 2010; and Department of Homeland Security, *The 2014 Quadrennial Homeland Security Review*, 2014.

281 The White House, Office of the Press Secretary, "Biodefense for the 21st Century," 2004.

282 The White House, Office of the Federal Register, "Directive on Medical Countermeasures Against Weapons of Mass Destruction," January 31, 2007.

283 The White House, *National Biodefense Strategy*, 2018.

284 Ibid.

285 Please see Subcommittee on Emergency Preparedness, Science, and Technology, *Hearing: Project BioShield: Linking Bioterrorism Threats and Countermeasure Procurement to Enhance Terrorism Preparedness*, 2005; Mark A. Randol, *Congressional Research Service Report - The Department of Homeland Security Intelligence Enterprise: Operational Overview and Oversight Challenges for Congress*, 2010; and Department of Homeland Security, "Biological Security," 2012.

286 Department of Homeland Security, *National Biosurveillance Integration Center Strategic Plan*, 2012.

287 Scott White, Department of Homeland Security, Science and Technology Directorate, *Presentation: CBRN Terrorism Risk Assessments, Methods and Applications*, 2016.

288 See K. Halliday, *Lawrence Livermore National Laboratory Report: Biodefense Knowledge Management System*, 2020 and Departments of Homeland Security and Justice, *Fusion Center Technology Guide: DHS/DOJ Fusion Process, Technical Assistance, Program and Services*, 2009.

However, past analyses of this infrastructure have criticized how these centers have operated, how they leverage data, and how products from them are subsequently used.[289]

DHS, in cooperation with interagency partners, should strongly consider conducting an assessment of its current operational and analytical processes and identify opportunities to streamline and filter data streams and information inputs, including to best separate signals from noise.

Further, DHS should take advantage of other advances in how the nation and international community work to understand biological threats---including if changes recommended in this report are implemented. Some could significantly shape the agency's threat awareness work in the years ahead. One example is the new forecasting and outbreak analytics center established at the Centers for Disease Control and Prevention (CDC) in 2021. Initially funded through the American Rescue Plan, this center will work on predicting disease outbreaks through modeling and forecasting capabilities, connecting public health and health security stakeholders, and informing stakeholders in the public and private sectors to galvanize action. DHS should consider innovative models for collaborating with this CDC center, potentially including colocating its own fusion centers like NBIC so that both agencies can maximize one another's contributions to the other (and to the full range of stakeholders in their threat assessment and forecasting work).

PREVENTION AND PROTECTION - BIO EXERCISES AS STRATEGIC ASSETS

DHS also funds programs, provides expertise, and builds relationships with stakeholders across the interagency and the private sector to prevent and protect against biological threats. Programs like the Buffer Zone Protection Program (BZPP) provide grants to states and local jurisdictions to secure critical infrastructure such as healthcare facilities.[290] DHS also provides educational opportunities such as in-person and online workshops for critical infrastructure and key resources (CIKR) facilities as a way to increase awareness and enhance resilience against biological and other threats.[291] For CIKR facilities that request it, DHS experts are available to conduct Site Assistance Visits and Critical Infrastructure Protection security surveys to find existing vulnerabilities and address them.[292] DHS S&T also works with external academic partners via its Centers of Excellence (COEs) program to leverage cutting-edge technologies and research in its efforts to better assess, prevent, protect against, monitor, and respond to biological threats.[293]

In terms of preparedness, DHS has long worked with local, state, and federal partners in exercises regarding biological threats via the National Exercise Program. Going forward, bio exercises need to continue---and be viewed as a strategic asset for U.S. deterrence against deliberate biological threats. Of course, such exercises can also benefit pandemic preparedness and foster the one-health approach to addressing biological risks.

Such exercises can signal to outside observers that the United States has anticipated, and is successfully prepared to respond to, biological attacks. This is more important than ever after the visible and tragic stumbles that occurred

289 U.S. Senate, *Committee on Homeland Security and Government Affairs, Permanent Subcommittee on Investigations Report: Federal Support for and Involvement in State and Local Fusion Centers*, 2012.

290 See Sandy Smith, "DHS Announces $91.3 Million in Buffer Zone Protection Program Grants," *EHS Today*, 2005; Department of Homeland Security, Office of Operations, "Appendix D. Funding and Responsibility Chart of U.S. DOT, U.S. DOJ, DHS/FEMA," 2010; and "Buffer Zone Protection Program," Federal Grants Wire, 2020.

291 Department of Homeland Security, "Office of Infrastructure Protection".

292 Please see Department of Homeland Security, "National Protection and Programs Directorate, Office of Infrastructure Protection, Activities in the U.S. Insular Areas of Guam, American Samoa, and U.S. Virgin Islands," 2009; Department of Homeland Security, Cybersecurity and Infrastructure Security Agency, "Assist Visits,"; and Department of Homeland Security, "Biological Security," 2012.

293 National Research Council, *University Research Centers of Excellence for Homeland Security: A Summary Report of a Workshop*, 2004.

BioWatch field operations in action. Department of Homeland Security

during COVID-19 responses. DHS can expand its incorporation of biological threats and responses into the National Exercise Program. It can also help ensure the progress made stemming from these exercises is telegraphed strategically and shared with the American people.

SURVEILLANCE AND DETECTION - ADVANCING NEW TECHNOLOGIES

DHS uses several methods to monitor and detect potential biological attacks on U.S. soil. S&T Programs like the Enhanced Passive Surveillance (EPS) project use information technology systems to acquire, integrate, and analyze real-time health surveillance data.[294] DHS S&T also contains outreach and research and development initiatives such as BioThreat Awareness APEX, a program that both engages state, local, and tribal jurisdictions to understand existing situational awareness capabilities via workshops and table-top exercises, and supports the development of real-time detection systems and infrastructure for biological attacks.[295] DHS has also researched, developed, and deployed a system known as BioWatch - an early warning system that uses a network of field detectors to sample the air, pick up pathogens of concern, and activate response protocols in the face of an offensive biological event.[296]

294 Institute for Infectious Animal Diseases at Texas A&M, *Enhanced Passive Surveillance Concepts of Operations (CONOPS) - Report from a Workshop Held as a Part of the "Towards Large-Scale Enhanced Passive Surveillance Project*, 2014.

295 See Department of Homeland Security, Science and Technology Directorate, "CBD Focus Areas - Biosurveillance," and Government Accountability Office, *Report to the Honorable Scott Perry - Homeland Security: Research & Development Coordination Has Improved, but Additional Actions Needed to Track and Evaluate Projects*, 2019.

296 See Department of Homeland Security, Office of Health Affairs, "BioWatch Fact Sheet," 2016; and Dana A. Shea and Sarah A. Lister, *Congressional Research Service Report - The BioWatch Program: Detection of Bioterrorism,* 2003.

DHS should explore new technologies and means to enhance early warning capabilities while minimizing the likelihood of false positives. One such technological system is known as Biological Detection for the 21st Century (BD21). This is intended to merge a variety of technologies together, including biological sensors, data analytics, collectors, field screening devices, and anomaly detection tools via algorithms to provide the functionality that BioWatch was intended to provide. It also is intended to take additional actions for even low-consequence responses such as diverting the airflow in buildings or blocking individuals from entering potentially contaminated locations.[297] As these complex technologies and systems are further researched, developed, and tested, it is also necessary to generate clear guidance and a robust implementation plan based on what the system detects and what is ultimately verified in the lab after subsequent testing and analysis.[298]

Policy makers should continue to support advances and exploration by DHS for optimal technological options to detect biological threats. In order for the nation to best leverage significant advances made in academia and private companies in recent years, DHS can help lead in testing to assess efficacy, maturity and implementation considerations, and in providing clear operational protocols regarding use of the knowledge gained from these technologies, such as in the event of a confirmed pathogen detection event.

Despite operational and procedural issues with the BioWatch program, it was a breakthrough in that it built a novel infrastructure of technology and people across the United States as a prototype of a domestic-based early warning system.[299] One of its main issues has been that it could not distinguish between a deliberate event and a pathogen of concern that may exist in the local environment where detection is being conducted. This inability to distinguish natural from deliberate served as a critical limiting factor.[300]

RESPONSE AND RECOVERY - TOWARD CUTTING-EDGE RESEARCH AND TALENT

DHS has a number of systems in place and resources for response and recovery from biological attacks. Efforts to protect first responders, law enforcement, and other stakeholders in contaminated environments include the efficacy assessment of powered air-purifying respirators (PAPRs) that are compatible with masks. The agency is exploring compact and next-generation personal protective equipment.[301] DHS also works with partners like the Metropolitan Transportation Authority New York City Transit to test and validate new technologies.[302] Further, DHS brings the National Bioforensic Analysis Center (NBFAC) to the table, which uses expertise and cutting-edge research technology to further its capabilities in both traditional forensics and bioforensics approaches to work toward tracing and attributing the source of biological attacks.[303]

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297 U.S. Government Accountability Office, *Report to Congressional Requesters: Biodefense - DHS Exploring New Methods to Replace BioWatch and Could Benefit from Additional Guidance*, 2021.

298 Ibid.

299 Government Accountability Office, *Report Before the Subcommittee on National Security, Committee on Oversight and Reform, House of Representatives: Biodefense - The Nation Faces Long-Standing Challenges Related to Defending Against Biological Threats,* 2019.

300 National Academies of Sciences, *BioWatch and Public Health Surveillance: Evaluating Systems for the Early Detection of Biological Threats*, 2011.

301 Please see Department of Homeland Security, "CBD Focus Areas - Response and Recovery"; Department of Homeland Security, "Powered Air Purifying Respirators Assessment: Law Enforcement Applications," 2007; and Department of Homeland Security, *After Action Report - Next Generation Personal Protective Equipment (PPE) Discussion Meeting*.

302 Melinda Moore, Eric Landree, Alison K. Hottes, and Shoshanna R. Shelton, *Environmental Detection and Human Biosurveillance Research and Development for National Security: Priorities for the Department of Homeland Security Science and Technology Directorate*, RAND Corporation's Homeland Security Operational Analysis Center, 2018.

303 James Burans, Jennifer Goodrich, Robert L. Bull, and Nicholas H. Bergman, "The National Bioforensic Analysis Center," *Microbial Forensics*, 2020: pp. 457 - 461.

The United States can further leverage unique DHS capabilities and expertise in the event of a biological attack on the United States and its allies. This includes bioforensics capabilities that are meant to characterize biological materials and accurately attribute the cause of a biological attack to its source. Further, given that the science and knowledge concerning the life sciences is rapidly changing, it is highly recommended that DHS components incorporate greater engagement with the broader scientific community, as well as attracting, retaining, and collaborating with the best and the brightest in the field.

As discussed in this roadmap's chapter on the Department of State and its role in addressing biological threats, attribution involves two components: a forensics component driven by science to trace an attack to its source, and the sociopolitical maneuvering that results as the validity of the attribution is debated.[304] While this dynamic means that bioforensics alone does not constitute attribution, it does not mean that leveraging new technological assets and developing new bioforensics tools is futile. Rather, increasing the efficacy and accuracy of bioforensics capabilities in spaces like DHS's National Biodefense Analysis and Countermeasures Center (NBACC) can function as a critical component of a deterrence strategy against biological weapons from both state and non-state actors.

Developing cutting-edge approaches and incorporating new technologies into bioforensics requires having access to the best and the brightest scientists and technicians across a variety of technical and social science disciplines, as well as analysts and logisticians to make sure these tools work in a real-world context. Part of gaining access to the best minds and talents lies in strengthening already-existing relationships between DHS and its academic partners via their Centers of Excellence program. Other means of supplementing expertise and talent at NBACC includes the use of contracting tools such as the Intergovernmental Personnel Act.[305]

CONCLUSION

As DHS continues to evolve, it is important to envision how its assets and capabilities can be better leveraged to address biological risks. In the years ahead, key actions can include ensuring that biological threat exercises are maximized for their value in both deterrence and pandemic prevention, maintaining high-level support for DHS advancing new and emerging technologies optimally, and envisioning new mechanisms for cooperation with emerging entities for early warning, forecasting, and biological threat analysis and awareness.

304 Jackson duPont, Yong-Bee Lim, Christine Parthemore, and Alexander Titus, *Key U.S. Initiatives for Addressing Biological Threats Part 4: The Department of State, Council on Strategic Risks*, 2021.

305 National Defense University, Center for Technology and National Security Policy, *Strengthening Government Laboratory Science and Technology Programs: Some Thoughts for the Department of Homeland Security*, by Samuel Musa, Richard Chait, Vincent Russo, and Donna Back, 2011.

The United States Department of Agriculture (USDA), which comprises nearly 30 agencies and offices, makes significant contributions to biological threat detection, response, and mitigation efforts at the intersection of plants, animals, and human health. Examples of the USDA's work against biological threats include the following.

The Animal and Plant Health Inspection Service (USDA-APHIS). USDA-APHIS holds sway and responsibility for a broad range of biological threat responses, including in animal health and welfare, invasive pests, animal and plant imports and exports, and research and development on biotechnologies with plant and animal implications. The USDA-APHIS is also the agency's lead for the Select Agent Program, which establishes and regulates a list of biological agents and toxins. USDA-APHIS may also play an even stronger role in pathogen early warning in the future as the lead agency for USDA biosurveillance. This work focuses on detecting SARS-CoV-2 and emerging, re-emerging, and other zoonotic diseases in susceptible animals.[306] A 2021 expansion of the program by $300 million should help improve early detection and response to zoonotic diseases.[307]

The Agricultural Research Service (USDA-ARS). The work of USDA-ARS is typically framed within the context of global food security, but the agency's work in prevention, detection, reporting, and control strategies related to countering plant and animal pathogens also overlaps in addressing biological threats. The USDA-ARS has extensive connections with the U.S. Department of State's Biosecurity Engagement Program. This program in conjunction with USDA-APHIS, are the leads for the National Bio and Agro-Defense Facility, a BSL-4 biocontainment laboratory that aims to replace the existing Plum Island Animal Disease Center.[308]

The Foreign Agricultural Service (USDA-FAS). This agency also engages in the global food security space, but its work on trade policy, market development, export assistance, and data and analysis leveraging USDA-FAS's market intelligence capacity, also have clear implications for addressing biological threats. In addition, given that FAS staffs 94 offices in 76 countries around the world, the direct input that this agency receives from its offices can contribute significantly to enhancing U.S. and global capabilities to address biological threats.

With these and other programs, the USDA's role in biological threat reduction extends to diplomacy, homeland security, and intelligence. On the diplomacy side, leveraging USDA assets for biosafety and biosecurity outreach helps build domestic and international capacity, as well as robust relationships between the United States and its partners. On the interagency side, USDA is well-connected with other departments in ways that are vital to addressing complex biological threats. Finally, on the intelligence side, having both domestic and international assets for information-gathering means that USDA is a major asset for accurate, real-time information when it comes to plant, animal, and potentially human health events.

306 U.S. Department of Agriculture, Animal and Plant Health Inspection Service, "USDA Announces Proposed Framework for Advancing Surveillance for SARS-CoV-2 and Other Emerging Zoonotic Diseases through the American Rescue Plan," August 24, 2021.

307 U.S. Department of Agriculture, Animal and Plant Health Inspection Service, "APHIS' American Rescue Plan (ARP) Surveillance Program: Strategic Framework," August 9, 2021.

308 U.S. Department of Agriculture, Agriculture Research Service, "National Bio and Agro-Defense Facility."

VI. DRIVING SYSTEMIC CHANGE[309]

As the prior chapters indicate, there are critical programs and robust capabilities across the U.S. government for addressing biological threats. The systemic change needed to significantly improve how the United States deters actors from pursuing and using biological weapons and preventing future pandemics will depend on how well it coordinates and integrates these governmental functions---and collaborates with nongovernmental and international actors.

This section shows how efforts to address biological threats cut across various agencies, and how they require that public and private sector visions and resources align. It also notes open questions that remain with regard to best promoting systemic progress.

First, it illustrates the multi-agency contributions that have facilitated the United States making game-changing advances in the rapid development of medical countermeasures.

Second, it describes data and technological opportunities, as well as open questions, regarding how advances in pathogen early warning for biodefense will be integrated with those made for public health purposes, given both the overlap and unique needs in each area.

Third, it proposes a new, multi-agency annual exercise program to foster continual improvement in translating early warning into rapid and strong responses in developing diagnostics and creating safe and effective countermeasures. These exercises would also provide a mechanism for continuing to hone aspects of a well-functioning system such as supply chain management, distribution, and communications.

These lines of effort all overlap and must be coordinated, including by the White House. Much of this work is already starting, as described in prior chapters, yet more work is needed for policy makers and the public to more easily understand the systemic changes that are underway and the potential impact this could have on mitigating the full range of biological risks.

309 Much of the text in this section is drawn directly from Yong-Bee Lim and Christine Parthemore, "Key U.S. Initiatives for Addressing Biological Threats Part 5: The Future Industrial Base for Rapid Medical Countermeasure Development," *Council on Strategic Risks*, September 6, 2021.

Navy Petty Officer 2nd Class Blythe Turney, a hospital corpsman at Walter Reed National Military Medical Center, receives a COVID-19 vaccination, Walter Reed National Military Medical Center, Bethesda, MD, Dec. 14, 2020.
Lisa Ferdinando/Department of Defense

RAPID DEVELOPMENT AND MANUFACTURING OF MEDICAL COUNTERMEASURES

As the global community continues to struggle with the COVID-19 pandemic, it must also prepare for subsequent infectious disease outbreaks, which many experts predict will occur more frequently in the decades ahead. Further, biological threats do not just emerge from nature; greater distribution of equipment, materials, and knowledge are lowering barriers for developing biological weapons, and advances in the specificity of biotechnology are potentially opening new avenues for novel biological threats.[310]

Fortunately, COVID-19 also accelerated significant advances in how we stop biological threats from creating mass harm. One of the most significant advances has been in the rapid development, manufacturing, and deployment of medical countermeasures.

In the United States, this work was driven by Operation Warp Speed (OWS), an effort predominantly between the departments of Health and Human Services (HHS) and Defense (DoD).[311] OWS leveraged interagency and public-private cooperation with judicious strategies to accelerate vaccine development, mitigate safety risks, and jump-start

310 Michael Moodie, "Chapter 14. Options and New Dynamics: Chemical and Biological Weapons Proliferation in 2020," in James W. Wirth and Peter R. Lavoy, *Over the Horizon Proliferation Threats* (Redwood City: Stanford University Press, 2020): pp. 266 - 290.

311 U.S. Department of Defense, "Coronavirus: Timeline," 2021.

commercial-scale manufacturing.[312] The accomplishments of this initiative are clear: the game-changing development and deployment of vaccines against COVID-19 in just 11 months after the genetic sequence for the virus that causes it was in the hands of researchers.[313]

It is critical to capitalize on the successes of OWS and apply lessons from the experience to improve the industrial base for producing medical countermeasures. OWS should serve as the new minimum baseline, building on it for increased speed, scaling, and resilience.

To this end, the U.S. government is setting strong goals, including the targets of having the "capability to design, test and approve safe and effective vaccines within 100 days of detecting a pandemic threat" and "manufacture enough doses to supply the world within 200 days."[314] These goals are achievable if the nation fosters a medical countermeasure ecosystem with core capacities and greater surge capacity---one that promotes diversity in the U.S. bioeconomy and resilience. Such an approach would simultaneously strengthen the U.S. ability to address all manner of biological threats, strengthen supply chains to minimize disruptions to valuable life sciences work, and even shrink target timelines towards life-saving medical countermeasures in adverse events.[315]

The following section provides background on OWS and factors that contributed to its success, and then proceeds to recommendations for improving capacity for rapid medical countermeasure development, production, and delivery for addressing the full range of biological threats.

OPERATION WARP SPEED (OWS)

There is no definitive timeline on the emergence of the SARS-CoV-2 virus. It was first reported in humans in December 2019[316] but may have been in circulation in the human population as early as October 2019. Its spread and severe symptoms led the World Health Organization (WHO) to declare COVID-19 a pandemic on March 11, 2020, with the United States declaring it a national emergency shortly afterwards.[317]

The U.S. government announced OWS in April 2020. Its aim was to bring the COVID-19 pandemic under control by accelerating the research, development, manufacturing, scaling, and distribution of vaccines, therapeutics, and diagnostics. Further, OWS was designed to put promising candidates through difficult hurdles while simultaneously walking their manufacturers through the FDA approval process. The end goal was to deliver tens of millions of effective and safe vaccines by the end of 2020, and as many as 300 million doses by mid-2021.[318]

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312 U.S. Government Accountability Agency, *Operation Warp Speed: Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*, 2021.

313 Helen Branswell, "12 Lessons COVID-19 Taught Us About Developing Vaccines During a Pandemic," *PBS News Hour*, 2021.

314 Eric Lander, "As Bad as COVID-19 Has Been, a Future Pandemic Could be Even Worse — Unless We Act Now," *The Washington Post*, 2021.

315 For examples, see Gerald L. Epstein, *Testimony before the Bioterrorism and Public Health Preparedness Subcommittee, Committee on Health, Education, Labor, and Pensions - Biodefense: Building a Medical Countermeasure Capability*, 2005; U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response, "HHS Takes Immediate Action to Secure Pharmaceutical Supply Chain," 2021; and Marcy E. Gallo, *Congressional Research Service - The Bioeconomy: A Primer*, 2021.

316 See Lauren M. Sauer, "What is Coronavirus?" *Johns Hopkins School of Medicine* and Scott LaFee, "Novel Coronavirus Circulated Undetected Months before First COVID-19 Cases in Wuhan, China," *University of California San Diego Health*, March 18, 2021.

317 "WHO Director-General's Opening Remarks at the Media Briefing on COVID-19 - 11 March 2020," *World Health Organization*, 2020 and "Proclamation 9994 of March 13, 2020: Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak," *Federal Register*, March 18, 2020.

318 Moncef Slaoui and Matthew Hepburn, "Perspective: Developing Safe and Effective Covid Vaccines - Operation Warp Speed's Strategy and Approach," *New England Journal of Medicine*, October 29, 2020.

This initiative was bold given the history of vaccine research and development. Vaccines historically have taken 10-15 years to develop. However, gene sequencing and synthesis technologies have become faster and cheaper in recent years, and disciplines like bioinformatics have enhanced researchers' ability to understand emerging infectious diseases.[319] Challenges lie more in coordination and regulatory processes which, done poorly, can stifle innovation and slow progress toward the completion of complex scientific tasks like vaccine development.[320]

OWS succeeded in the rapid development, safety and efficacy testing, and manufacture of five vaccine candidates. In terms of development, OWS sought to minimize risk and maximize success by selecting vaccine candidates that stimulate immunological responses against COVID-19 through different mechanisms. In terms of safety and efficacy, OWS took steps to accelerate the clinical trial and review process by relying on data from other vaccines that used the same platforms and conducting animal studies alongside clinical trials (rather than the normal process of these steps being sequential). Vaccine candidate companies also began large-scale manufacturing during clinical trials---supported by government purchase orders---to ensure that the production capacity was there as soon as their vaccines received emergency use authorization (EUA) from the Food and Drug Administration (FDA).[321] The U.S. government also used advanced purchase contracts to ensure manufacturers had a clear market incentive to do this vaccine work.[322] By January 2021, OWS officials reported that vaccine companies had produced and released 63.7 million doses of vaccine.[323]

Three factors facilitated the U.S. government and private partners in achieving this unprecedented outcome. First, the severity and scope of COVID-19 raised it to the top of the priority list for many countries, including the United States, and created the collective political will needed to surge resources. This allowed for fast policymaking and helped the federal government meet the challenges of inadequate supply chains while researching, developing, testing, and producing diagnostics, therapeutics, and vaccines for COVID-19.

Of particular note were the Coronavirus Preparedness and Response Supplemental Appropriations Act of 2020 and the Defense Production Act. These policies simultaneously provided funding for HHS activities related to COVID-19 and allowed the U.S. government to pivot and address shortages in response-related materials ranging from personal protective equipment to essential reagents for diagnostics and therapeutics.[324]

Second, OWS was built on past successes and experiences with other infectious disease events, including the 2014-2017 Zika epidemics. These experiences helped galvanize an integrated structure for COVID-19 countermeasure research that included capabilities and expertise from private industry, as well as government assets across the Department of Health and Human Services, the Department of Defense, the National Institutes of Health, and other agencies.[325]

Third, OWS leveraged decades of research and development that led to platform technologies for the development of vaccines and other countermeasures. One platform type that showed significant potential was based on the much-

319 National Research Council, *The Genomic Revolution: Implications for Treatment and Control of Infectious Disease: Working Group Summaries*, November 10 - 13, 2005.

320 See Heidi Legg, "Interview with Kendall Hoyt," and Mark Toshner, "Less Than a Year to Develop a COVID Vaccine - Here's Why You Shouldn't Be Alarmed," *The Conversation*, November 25, 2020.

321 U. S. Government Accountability Office, *Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*, 2021.

322 Simi V. Siddalingaiah, *Congressional Research Service - Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccination Materials*, 2021. Note: Pfizer produced an additional vaccine candidate now in use without using all available government financial incentives.

323 U. S. Government Accountability Office, *Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development*, 2021.

324 For examples, see Anshu Siripurapu, "What is the Defense Production Act?" *Council on Foreign Relations*, 2021; U.S. Government Accountability Office, *Defense Production Act - Opportunities Exist to Increase Transparency and Identify Future Actions to Mitigate Medical Supply Chain Issues*, 2020; and the United States White House, *National Strategy for the COVID-19 Response and Pandemic Preparedness*, 2021.

325 Slaoui and Hepburn, "Perspective: Developing Safe and Effective Covid Vaccines."

studied and well-understood biological component known as messenger ribonucleic acid (mRNA). Scientists have studied mRNA since the 1970s, resulting in the robust characterization of this mechanism that bridges the gap between protein-encoding DNA and the actual production of cellular proteins.[326] Additionally, mRNA vaccines have been tested and used in animal populations with promising results against maladies ranging from cancers to infectious diseases.[327] Platforms based on mRNA and other mechanisms can now be used to produce the key ingredients of vaccines with speed and great consistency.

THE FUTURE MEDICAL COUNTERMEASURE ECOSYSTEM

Both the technologies and expert experiences that made Operation Warp Speed (OWS) transformative were built on decades of efforts and investments. Now, the OWS approach must become the new minimum baseline from which the United States and other nations reshape their bio-industrial bases in order to prevent future pandemics and deter the use of biological weapons.

In this context, the United States should take an ecosystem approach to encouraging a strong industrial base for rapid countermeasure development, manufacturing, and deployment. To this end, public and private sectors must map and update the landscape of available capacities, supply chains, and expertise on a regular basis.

This ecosystem will look different in the future than it has in the past. Greater roles will go to mRNA and other platform technologies, and cell-free manufacturing approaches that proved to be reliable and time-saving in COVID-19 countermeasure development. Supply chain bottlenecks have proven that capacity and redundancies to quickly produce consumables will be critical to rapid and effective responses to pandemic-potential pathogens. COVID-19 responses also showcased the growing role of machine learning and artificial intelligence, and helped inspire and expand start-up companies focused on designing systems to quickly identify existing therapeutics and vaccines that could help address newly-concerning disease threats, including drugs that may already be tested and approved for other purposes.

As such, **the broad U.S. bioeconomy should be considered a strategic asset capable of surge capacity to quickly and effectively respond to novel infectious disease threats.** This requires constant support of the infrastructure and supply chains that expanded in response to COVID-19.

Sustained support for DoD and HHS Advanced Development and Manufacturing (ADM) facilities is a key aspect of this recommendation. ADM facilities have faced many challenges in the past, including financial sustainability issues. During the COVID-19 pandemic, the facilities were forced to troubleshoot through the ambitious, first-ever scale and speed of production that Operation Warp Speed required. Lessons from that fast ramp-up must inform plans for maintaining the longevity of these facilities. This should include creative and revenue-generating approaches, including annual exercises and steady-state processes recommended below, as well as diversifying the portfolio of ADM facilities to include biomanufacturing and other projects that contribute to the U.S. bioeconomy.

In addition to fixed assets such as ADMs, significant COVID-19 response capacity came from academic labs, the U.S. National Labs, nonprofits, and private companies pivoting their existing assets to aid in testing, data collection and

326 Norbert Pardi, Michael J. Hogan, Frederick W. Porter, and Drew Weissman, "mRNA Vaccines - A New Era in Vaccinology," *Nature Reviews Drug Discovery* Vol. 17, 2018: pp. 261 - 279.

327 Ibid.

sharing, production of consumables, and other functions.[328] These assets need to be maintained and incentivized to pivot toward rapid and robust outbreak responses in the future. Multipurpose biofoundries located in geographically dispersed cities should also be part of this bioeconomy surge capacity.[329] This will naturally entail some updates to the authorities and resources of key U.S. departments and agencies.

COVID-19 also showcased how interconnected and international supply chains are, especially for large-scale vaccine production. Fostering a healthy supply base within the United States, in particular for some critical materials like reagents and enzymes, is a required step to address this. The U.S. also needs to take a global leadership perspective to fix the supply chain issues that hampered COVID-19 responses. Diplomacy and expanded trade relationships must be part of the solution, just as DoD supports a multinational industrial base with international partners and allies contributing to logistics, co-manufacturing, and readiness for wide-ranging crises.

A strong core of domestic development and manufacturing assets, a healthy bioeconomy ready to surge to help quash infectious disease outbreaks, and strong international partnerships can provide sufficient assets to allow the United States to experiment with and refine approaches to biological threat prevention and preparedness such as virtual stockpiling, best uses of the Defense Production Act, and rapid response funding and business models.

New, small, and innovative companies will become increasingly central features of the U.S. rapid medical countermeasures ecosystem. Though the medical countermeasure landscape is still characterized by large-scale IT, consulting, and pharmaceutical companies, that landscape was already evolving in advance of the COVID-19 pandemic.[330] OWS experiences highlighted that the complexity of navigating federal contracts makes it difficult for any but the largest and most well-resourced private companies to contribute.[331] Moving forward, the U.S. government must **improve its ability to work with younger, innovative companies and small businesses.**

Some hurdles are financial. Newer companies at times rely on Small Business Innovation Research (SBIR) funds for early-stage research. Yet SBIR grants are incredibly small and often do not cover the costs of conducting the research the U.S. government seeks to foster. Further, for start-up companies that do seek SBIRs, these funds may not become available until the long process of review and approval is complete; there are even circumstances where successful start-ups may no longer even require the SBIR they applied for. These issues lead many small and new businesses to rely on nongovernmental financing, which can exacerbate the issues of companies doing well but not producing what the U.S. government needs for purposes like strong biological event responses, and U.S. officials at times not having access to cutting-edge technology developments and trends.

Increasing the size of SBIR grants, as well as streamlining the timeline it takes to review and approve such grants, would help. Breaking government projects into smaller scopes of work that are better integrated by government

328 For examples, see Anup Singh, Christine Parthemore, and Andrew Weber, *Making Bioweapons Obsolete: A Summary of Workshop Discussions*, 2019, and *Critical Steps in Preventing Future Pandemics*, 2021, both published by the Council on Strategic Risks and Sandia National Laboratories.

329 For examples, see Nathan Hillson, Mark Caddick, Yizhi Cai, Jose A. Carrasco et al., "Building a Global Alliance of Biofoundries," *Nature Communications* Vol. 10, Article 2040, 2019; United States Department of Commerce - National Institute of Standards and Technology, "The NIST Biofoundry: Taking Engineering Biology from Artisanal to Automated," 2020; and Melody M. Bomgardner, "Ginkgo Opens Facilities to Help COVID-19 Coronavirus Response," *Chemical and Engineering News*, 2020.

330 Chad P. Bown and Thomas J. Bollyky, "How COVID-19 vaccine supply chains emerged in the midst of a pandemic," *Peterson Institute of International Economics*, 2021.

331 The listings of top OWS contracts for COVID-19 vaccines and ancillary vaccination materials contain highly-established companies, as opposed to small-scale or start-up biotech companies. The U.S. Committee on Small Business and Entrepreneurship realizes this is an issue. Some attribute this inequity to the bandwidth constraints that small businesses face when applying for federal government grants. For examples, see United States Congress, Senate Committee on Small Business and Entrepreneurship, "Issues," and Geoff Orazem, Greg Mallory, Matthew Schlueter, and Danny Werfel, "Why Startups Don't Bid on Government Contracts," *Boston Consulting Group*, August 22, 2017.

personnel and expanding requirements for small-business consortiums and sub-contracts by larger companies are also commonly-used techniques that can be applied to the bio industrial base. However, it is critical that such measures are used to foster and de-risk innovative countermeasure developers rather than perpetuate outdated tools and methods. Eliminating funding requirements that are overly-biased toward the largest companies (e.g., recent BARDA requests that require existing, large-scale countermeasure manufacturing capacity) will also be important and increasingly feasible as manufacturing methods change and as a more diverse and interconnected ecosystem fosters broader partnership options.

Other hurdles stem from a lack of public-private interactions. Promising entrepreneurs and technologists may not know how to collaborate with U.S. departments and agencies unless their network includes people with knowledge of how the U.S. government works. Establishing and maintaining better networks across public and private sectors in advance of a biological event is crucial---a capacity we are developing at the Council on Strategic Risks through the Alliance to End Biological Threats and other projects.[332] Other initiatives also hold great promise, such as a Biosecurity Reserve Corps proposed in this handbook in which nongovernmental experts could serve short stints at the National Labs or within DoD and HHS for networking, collaboration, and surge preparedness purposes.[333]

Additionally, **the U.S. government must set guidance for early warning signals triggering medical countermeasure and diagnostic development responses.** This guidance must accompany the ongoing U.S. and international development of pathogen early warning and disease forecasting systems, and indicate the conditions when senior leaders should approve the ramp-up of identification and development of therapeutics, vaccines, and diagnostics.

While some nations such as South Korea developed diagnostic tests within weeks of their COVID-19 outbreaks starting, this took the United States several months. A core mechanism for improving this is to ensure that U.S. leaders have the authorities and resources needed to trigger the initiation of countermeasure and diagnostic development early after a pathogen of high concern is identified, or when an outbreak originating in another country is clearly underway.

Triggering development and production processes earlier in responding to infectious disease threats will naturally take dedicated funding, just as the nation continually resources response infrastructure that Americans take for granted, such as fire departments. Similar to how many nations maintain preparedness for natural disasters, the United States should **launch an annual exercise program to practice and improve countermeasure development and production.** This can help keep the medical countermeasure ecosystem prepared for emergencies and be used to identify gaps and methods for improvement in advance of the next biological event. A strong goal would be to use this exercise program to halve the time that OWS took to produce COVID-19 vaccines.

Additionally, the nation can **use expanded production capacities catalyzed by COVID-19 to help bring existing, promising medical countermeasure candidates across the line of FDA approval.** HHS and DoD have invested in early-stage research and development of several candidate therapeutics and vaccines for diseases of concern to the U.S. public and military forces. When the current drive to produce COVID-19 vaccines subsides, the nation can use these assets to produce sufficient doses for any clinical trials needed for these already-invested candidates to be approved.

The nation used an analogous process to authorize Ebola vaccines and treatments. When the West Africa Ebola crisis hit in 2014-16, the Department of Defense (DoD) used its prior research and development of Ebola countermeasures to bring strong candidates closer to FDA approval. When the epidemic subsided, pharmaceutical companies lost interest. Creative military and civilian personnel in DoD and HHS helped ensure these Ebola countermeasure

332 The Council on Strategic Risks, "The Alliance to End Biological Threats."

333 Chris Fall, Yong-Bee Lim, and Christine Parthemore, *Key U.S. Initiatives for Addressing Biological Threats Part 2: The U.S. Department of Energy National Laboratories, Council on Strategic Risks*, 2021; and Trent Northen, Nancy Hagel, Daniel Sinars, Johnny Green, Dawn Wellman, and Daniel T. Schwartz, *Attracting and Retaining Top Scientists and Engineers at U.S. National Laboratories and Universities: Listening to the Next Generation*, 2018: pp. 1 - 6.

investments did not languish. The result was approved vaccines and therapies in use today to help quash regular Ebola outbreaks before they cause mass devastation. Notably, offices and individuals involved in this effort leveraged learnings from the process in creating Operation Warp Speed (OWS). Making this a standing, annual process (e.g., with a yearly target of at least one new FDA-approved vaccine or therapeutic) will create good jobs, ensure the nation can capitalize on past early-stage research and development investments, and showcase a world-leading U.S. ability to quickly bring countermeasures for infectious disease threats to fruition.

If U.S. capacities expand and evolve as outlined here, **it will change the landscape of threats to that infrastructure, and responses must outpace these threats.** With OWS, federal law enforcement and the intelligence agencies flagged that nation-states were targeting COVID-19 research organizations. In May 2020, the U.S. government issued a statement warning that organizations working on COVID-related research were being targeted by cyber actors and collectors associated with the People's Republic of China.[334] A few months later, additional intelligence revealed that Russian intelligence services were targeting American, British, and Canadian COVID-19 research and vaccine development sites.[335] Mitigating these attacks requires thoughtful, layered action on the part of the United States and its private sector collaborators.

Increasing countermeasure development and production speed is critical for preventing future pandemics and deterring biological weapons production and use. Due to innovations like those highlighted in this report, the regulatory process is now one of the longest and most daunting aspects. **OWS should be further mined for lessons on producing safe and effective countermeasures faster.** Having registries for clinical trials that capture the population diversity needed and more regular dialogue regarding standards and needs among the FDA, HHS, DoD, and others will help.

Finally, **the rapid medical countermeasures industrial base the United States fosters should be designed to be flexible and agile.** Changes in development and production methods will continue to occur. Some will be game-changing, such as the movement toward skin patches and oral doses of vaccines and medications. This would significantly change the demand for many supplies (such as sterile glass vials) and the still-long and technically-precise fill-and-finish process of getting vaccines into safe vials and ready for distribution. OWS demonstrated that steering this kind of change into significantly enhanced national preparedness for infectious disease threats will pay dividends in lives saved and jobs created.

CONCLUSION

OWS overcame significant challenges to ultimately succeed in the rapid development, production, and scaling of vaccines, therapeutics, and diagnostics. These challenges included initial limitations in manufacturing capacity, disruptions to manufacturing supply chains due to the global pandemic, and gaps in the hiring and training of personnel with the specialized skills and knowledge required for successful facility management and COVID-19 vaccine production.[336] In the years ahead, the United States must hold OWS as the new minimum standard and continue to develop systems for even better and more rapid advancements of medical countermeasures.

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334 The Federal Bureau of Investigation and The Department of Homeland Security, Cybersecurity and Infrastructure Security Agency, "Public Service Announcement: People's Republic of China (PRC) Targeting of COVID-19 Research Organizations," 2020.

335 National Security Agency/Central Security Service, "NSA Teams with NCSC, CSE, DHS-CISA to Expose Russian Intelligence Services Targeting COVID-19 Researchers," 2020.

336 U.S. Government Accountability Office, *Report to Congressional Addressees: Operation Warp Speed - Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*, 2021.

Col. Scott Coradi, (left) 111th Medical Group Commander and medical advisor for Pennsylvania Task Force South, trains members of Task Force Ghostrider, Spc. Dominique Dalessio (center) and Sgt. Shane Brandes (right) on proper procedures how to administer a COVID-19 test in Lancaster, Pa., on May 19, 2020. Under guidance from the Pennsylvania Department of Health, and monitored by CDC officials, Pennsylvania National Guard members with Task Force Ghostrider launched a point prevalence sampling strike team in Lancaster. The mission is designed to identify possible risks of exposure to COVID-19 by testing the entire staff and residents for the virus. This is the first in the pilot program that will reach out across the state. Master Sgt. George Roach/U.S. Air National Guard

EARLY WARNING FOR BIODEFENSE

Due to the COVID-19 pandemic, the international community is coalescing around the need for a global early warning system for biological threats and is beginning to take action. Already, nongovernmental organizations such as the Milken Institute and the Rockefeller Foundation, in addition to the Council on Strategic Risks (CSR), have put forth proposals as to what the future of pathogen early warning should look like. The World Health Organization (WHO), with the United Kingdom and Germany, have opened hubs for pandemic and epidemic intelligence. What will the expansion of broad-based early warning mean for the U.S. Department of Defense (DoD) and other agencies whose missions include addressing deliberate biological threats?

This question has yet to be fully answered. Moreover, the COVID-19 pandemic has coincided with a DoD push to better unify department-wide biosurveillance and early warning-relevant programs. The pandemic has also triggered broader improvements in U.S. early warning programs, such as the establishment of the Center for Forecasting and Outbreak Analytics at the U.S. Centers for Disease Control and Prevention (CDC), into which biodefense-focused early warning assets will have to integrate.

Moving forward, U.S. biodefense early warning efforts should build on DoD's strong history of work in this field, optimize its use of new and emerging technologies that are especially well-suited for its needs, and be designed to tie into a broader global early warning system focused on all sources of biological threats. This section briefly explores these topics, with a primary focus on DoD.

A BRIEF HISTORY OF BIODEFENSE BIOSURVEILLANCE & EARLY WARNING

DoD has a longstanding and significant role in addressing infectious diseases that predates the establishment of both the CDC and the WHO. One of its initial forays into biodefense can be characterized as research on military medicine: more than one hundred years ago, Walter Reed, a U.S. Army officer, helped confirm the theory that yellow fever is transmitted by the *Aedes* spp. mosquito. This increased confidence in U.S. forces operating safely in tropical zones and thereby facilitated the advancement of the Panama Canal.[337]

The early part of the 20th century witnessed the start of the "DoD laboratory," shorthand for the creation of laboratory capabilities within the United States and around the world to support biodefense. (See the text box on page 55 highlighting examples of such laboratories). Over time, DoD has leveraged this laboratory capacity in major efforts in research and medicine including responses to (viral) hepatitis A and E, influenza, antimalarials, and HIV, to name just a few examples.[338]

The role of DoD in biodefense has evolved since its earliest military medicine and laboratory expansion days. In the middle of the 20th century this was shaped by both warfare around the world and biological weapons activities by the United States and other nations. Biodefense needs have changed over time along with the character and locations of conflict, changes in disease trends generally, and diplomatic agreement by most nations to ban biological weapons and the correlated end to most nations' programs. For the United States, President Nixon's 1969 end to the U.S. offensive biological weapons program shifted the nation's work solely into the category of defensive efforts.

Today, DoD biodefense activities have wide-ranging utility spanning force health protection, biological weapons defense, and contributions to global health security. Across these functions, DoD has also long been a leader in advancing technologies to prevent, detect, and respond to biological threats. All three of these focus areas are critical in biodefense.

Contributing across all three functions, DoD has long been a leader in developing technologies to edge ever closer to pathogen early warning, with an aim to developing pathogen-agnostic systems. As early as the 1990s, DoD funded the development of tests for environmental monitoring that could detect up to ten pathogens at a time, including plague and Ebola, and funded specific military personnel to conduct these tests. DoD has also shared these sorts of capabilities with its allies and partners around the world over the course of decades, notably through the Biological Threat Reduction Program (BTRP) and the Able Response exercises to enhance South Korean capabilities against biological attacks that were outlined through this report.

337 Patrick Feng, "Major Walter Reed and the Eradication of Yellow Fever," *Army Historical Foundation*, accessed November 29, 2021.

338 Department of Defense, Walter Reed Army Institute of Research (WRAIR), "U.S. Military HIV Research Program," August, 2017.

PAST ADVANCES IN BIOSURVEILLANCE AND EARLY WARNING

DoD's decades of history in biosurveillance innovation have played an important role in shaping the path toward early warning that society is pursuing today. The following paragraphs provide a high-level overview of this work with examples of some of its key components.

To begin, it is noteworthy that DoD has significant repositories of health-related data for service members and beneficiaries, as consistent data over time is a valuable asset for pathogen and disease early warning.[339] These include both cross-sectional and longitudinal data that make up part of the Military Health System, as well as multiple systems focused on potential and confirmed exposures to toxins and other health dangers within the United States and around the world. The routine and *ad hoc* capture of health-related data on DoD populations is unlike any such data of its kind. DoD's systems combine inpatient and outpatient encounter data for each DoD person; pre-deployment, post-deployment, and routine physical assessments; and environmental health-related data (not tied specifically to a person). When these datasets are appropriately managed and their data interrogated, the resulting biosurveillance capability is impressive.

DoD has advanced several programs and efforts to develop new tools to best leverage these rich data sources since the 1990s. In 1996, in response to the Presidential Decision Directive NSTC-7 on addressing emerging infectious disease threats, DoD established the Global Emerging Infections Surveillance (GEIS) program, designed to support surveillance and outbreak response efforts in critical infectious disease focus areas.[340] GEIS focus areas were developed in concert with global combatant commands and became known as GEIS pillars. They included respiratory infections, febrile and vector-borne infections, enteric infections, and antimicrobial resistant infections (including sexually transmitted infections). GEIS has helped advance capabilities for rapid detection and characterization of endemic and emerging threats to military forces. Part and parcel of these efforts is to drive an understanding of the clinical and epidemiological characteristics of infectious diseases in order to produce actionable information for DoD and national decision makers.[341]

In 2004, DoD began developing a syndromic surveillance system aiming to use health indicators to catch disease threats as soon as possible, often earlier than traditional laboratory and clinical approaches can diagnose a specific disease. This work became known as ESSENCE: the Electronic Surveillance System for the Early Notification of Community-based Epidemics.[342] ESSENCE was designed as a pathogen-agnostic family of systems. It uses outpatient information to monitor trends and increases in activity that may represent a disease outbreak; a chemical, biological, radiological, or nuclear event; or other significant medical events. ESSENCE was one of the first syndromic surveillance systems developed, and became the basis for the same type of system now used in civilian health departments across the United States. The power of the system for pathogen early warning is increased with multiple data sources and good protocols guiding the use of system outputs. While its utility today is more for localized public health responses than for true early warning,[343] its advent by DoD represented an important step in the right direction.

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339 National Academies of Sciences, Engineering, and Medicine, *Perspectives on the Department of Defense Global Emerging Infections Surveillance and Response System* (Washington, DC: National Academy Press, 2001) and Melinda Moore, Gail Fisher, and Clare Stevens, *Report: Toward Integrated DoD Biosurveillance: Assessment and Opportunities*, RAND, 2013.

340 U.S. Department of Defense, Military Health Systems, "Global Emerging Infections Surveillance," and U.S. White House, Office of Science and Technology Policy, "Fact Sheet for Addressing the Threat of Emerging Infectious Diseases (Presidential Decision Directive NSTC-7)," June 12, 1996.

341 U.S. Department of Defense, Defense Health Agency, "Global Emerging Infections Surveillance," accessed November 29, 2021.

342 U.S. Department of Defense, Defense Health Agency, "Electronic Surveillance System for the Early Notification of Community-based Epidemics," accessed November 29, 2021.

343 Natasha E. Bajema, William Beaver, and Christine Parthemore, *Toward a Global Pathogen Early Warning System: Building on the Landscape of Biosurveillance Today*, Council on Strategic Risks, 2021: pp. 26 - 33.

Oxford Nanopore miniature sequencing device the MinION. Oxford Nanopore's technology has potential to be especially useful to detect novel pathogens. CIROSANTILLI2/WIKIMEDIA

Close up of the wearable health tracker Oura Ring. DTRA-JSTO is applying the commercial technology, such as the Oura Ring, for early detection of COVID-19 cases. TIMO/FLICKR

As active duty service members are deployed globally, DoD personnel have an inherently higher risk of exposure (including to unknown pathogens or toxins) than most U.S. citizens, and therefore must lean forward to be better prepared for responding to biological threats. One example of the higher risk experienced by the DoD, as well as the need for greater early warning capability, was the U.S. response to the influenza A/H1N1pdm09 virus. In Spring 2009, at the outset of the outbreak, the DoD laboratory capability for understanding the novel influenza virus was inadequate. Although DoD labs were the first in the world to detect the novel virus, viral samples from the first cases detected (in San Diego and Texas) had to be sent to the CDC for full characterization. While this happened within days thanks to existing strong collaboration on influenza between DoD and CDC, a better DoD capability for detailed viral characterization (subtyping and sequencing) would have supported and enhanced early warning. Further, after characterization of the novel pandemic influenza, DoD was reliant on the CDC for assays to test for the novel viral strain, further delaying appropriate diagnoses for active-duty service members in the United States and overseas.[344] This experience contributed to DoD leaders pushing for stronger innovation toward early warning and for greater investments in laboratories and other supporting infrastructure.

344 For examples, see U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "Morbidity and Mortality Weekly Report (MMWR) Update: Swine Influenza A (H1N1 Infections --- California and Texas," April 24, 2009; U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "Morbidity and Mortality Weekly Report (MMWR) Update - Swine Influenza A (H1N1) Infection in Two Children --- Southern California, March-April 2009," April 21, 2009; U.S. Department of Health and Human Services, "An HHS Retrospective on the 2009 H1N1 Influenza Pandemic," June 15, 2012; and the personal experience and expertise of some of the authors involved in H1N1 response and operations.

In 2009, the Defense Threat Reduction Agency's Joint Science and Technology Office launched another key step toward early warning with the Biosurveillance Ecosystem, or BSVE. The BSVE vision was expansive: it was designed to be a pathogen-agnostic, virtual, customizable, collaborative system that would advance DoD's use of commercial and government technologies to aggregate and analyze data streams. The BSVE would ingest a wide variety of data sources---open-source data, social media and diagnostic data, and DoD, interagency, national, and international surveillance system data---and provide actionable information to users. The BSVE was an early attempt at providing relevant biosurveillance information through data integration, second-wave AI, and protocols that would lead to enhanced situational awareness and actionable information.[345] It was developed over time in coordination with other U.S. government agencies and advanced in a manner that allowed key allied nations to use the system as well.[346]

This was accompanied by several other advances and new tools. In 2014, the DoD Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND) began creation of the Biosurveillance Portal based on the needs of the Special Operations Command. The Biosurveillance Portal aimed to be an unclassified visualization tool---a pathogen-agnostic system of systems intended to pull in capabilities and data streams that were already available across DoD, other government agencies, and industry in an easy to understand format. Designed for use by different DoD actors with wide-ranging needs, unlike the BSVE, the Biosurveillance Portal was designed for use with only minimal analytic training and much less technological sophistication.[347]

Around the same time, the U.S. Army Edgewood Chemical Biological Center and JPEO-CBRND collaborated on the development of the Joint United States Forces Korea Portal and Integrated Threat Recognition, or JUPITR, system. JUPITR was designed as a pathogen agnostic program to provide unique and stronger biological detection and early warning capabilities on the Korean Peninsula. The JUPITR program introduced new instrumentation, including commercial off-the-shelf biological detection systems that would increase the speed and ease of use of biosurveillance equipment for the United States Forces Korea.[348]

At the same time, the Defense Health Agency was advancing still other biosurveillance capabilities focused more on general defense health than the aforementioned tools that also carried unique requirements for early warning of biological weapons threats. In 2012, the Division of Integrated Biosurveillance (DIB) within the Defense Health Agency was established.[349] Similar to GEIS, the DIB is organizationally housed at the Armed Forces Health Surveillance Center and helps to coordinate DoD medical and public health information. DIB was designed to coordinate inputs across DoD, and with interagency and international inputs, and focused on two thrusts: 1) an Alert and Response operational capability intended to provide better situational awareness of health threats to the military; and 2) an Innovation and Evaluation capability to support future DoD biosurveillance technical needs, including testing and evaluating nascent capabilities that could ultimately lead to a fusion of data and information to inform actions and guidance.[350]

As the landscape of disease threats that may affect DoD personnel changes, alongside the emergence of even more powerful technologies to address them, DoD continues to reshape its work on early warning. This extends to further innovation in the supporting tools that will drive the richest possible data to pull into such systems. These efforts include the DoD Next Generation Sequencing and Bioinformatics Consortium established as part of the GEIS

345 Cheryl Pellerin, "DTRA Scientists Develop Cloud-Based Biosurveillance Ecosystem," *U.S. Department of Defense*, February 29, 2016.

346 Ibid.

347 Janelle A. Anderson, C. Nicole Rosenzweig, Jason Roos, and Brandon Flores, "The Global Biosurveillance Portal: Biosurveillance for the Department of Defense," *Online Journal of Public Health Informatics* 7, No. 1 (2015).

348 ECBC Communications, "JUPITR program takes shape on Korean Peninsula," *U.S. Army*, March 13, 2014.

349 Melinda Moore, Gail Fisher, and Clare Stevens, "Toward integrated DoD biosurveillance: assessment and opportunities," *Rand Health Quarterly* 3, No. 4 (2014).

350 Ibid.

program. GEIS used its network to help coordinate and improve pathogen sequencing and analysis efforts across DoD laboratories around the world. This Consortium has proven extremely helpful in response to the COVID-19 pandemic, with DoD labs able to pool resources and capabilities to swiftly "isolate the virus, share samples, and compare lab methods to improve their sequencing capabilities."[351]

In September 2020, DoD issued a directive updating how the department will organize its biosurveillance activities. While it did not provide detailed programmatic instructions, it should facilitate the department's responses to evolving disease threats, the technological changes that are emerging to create far-improved early warning, and the need to integrate biodefense assets alongside the vast advancements occurring in early warning worldwide.

BIODEFENSE NEEDS AND TECHNOLOGIES FOR EARLY WARNING

Some challenges to effective early warning stem from the need to integrate numerous data sources and types, such as clinical information, diagnostic tests, and environmental monitoring. At the same time, such work is at an exciting inflection point given that a range of new sources for improving early warning are coming into use or advancing in their development. Broader advances in biodefense technologies may also contribute to enhanced early warning in the years ahead, ranging from drones to sense biological and chemical threats, to advanced analytical systems, to protective equipment and wearables that can detect and transmit relevant information.[352]

Of the tools that DoD may create or adopt in the years ahead that may further advance early warning, some will also be deployed for broad public use, and some will need to be tailored for unique biodefense needs. These needs include adaptability for unique use settings and conditions, timelines, and disease threats.

Some technologies DoD will need are likely to carry unique requirements for their operational settings. Biodefense entities have long worked to develop diagnostic tools that can be maximally useful in remote settings far from traditional laboratory equipment, products that minimize cold-chain requirements and supplies like reagents, assets that weigh less or require less training for use, and tools that can transmit data well in areas lacking robust telecommunications systems.

Shortening timelines for detecting and understanding a disease threat can also be crucial for force health and biodefense purposes. Early warning for biodefense must aim to account for use in wartime scenarios in which conflict drives much behavior, and where general public health infrastructure that normally contributes to early warning may be overwhelmed or damaged. Tools in use must aim to protect relatively fixed assets such as bases and embassies as well as personnel in movement. For military purposes, understanding if a biological event is deliberate and working to attribute its sources become even more important for decision-making.[353]

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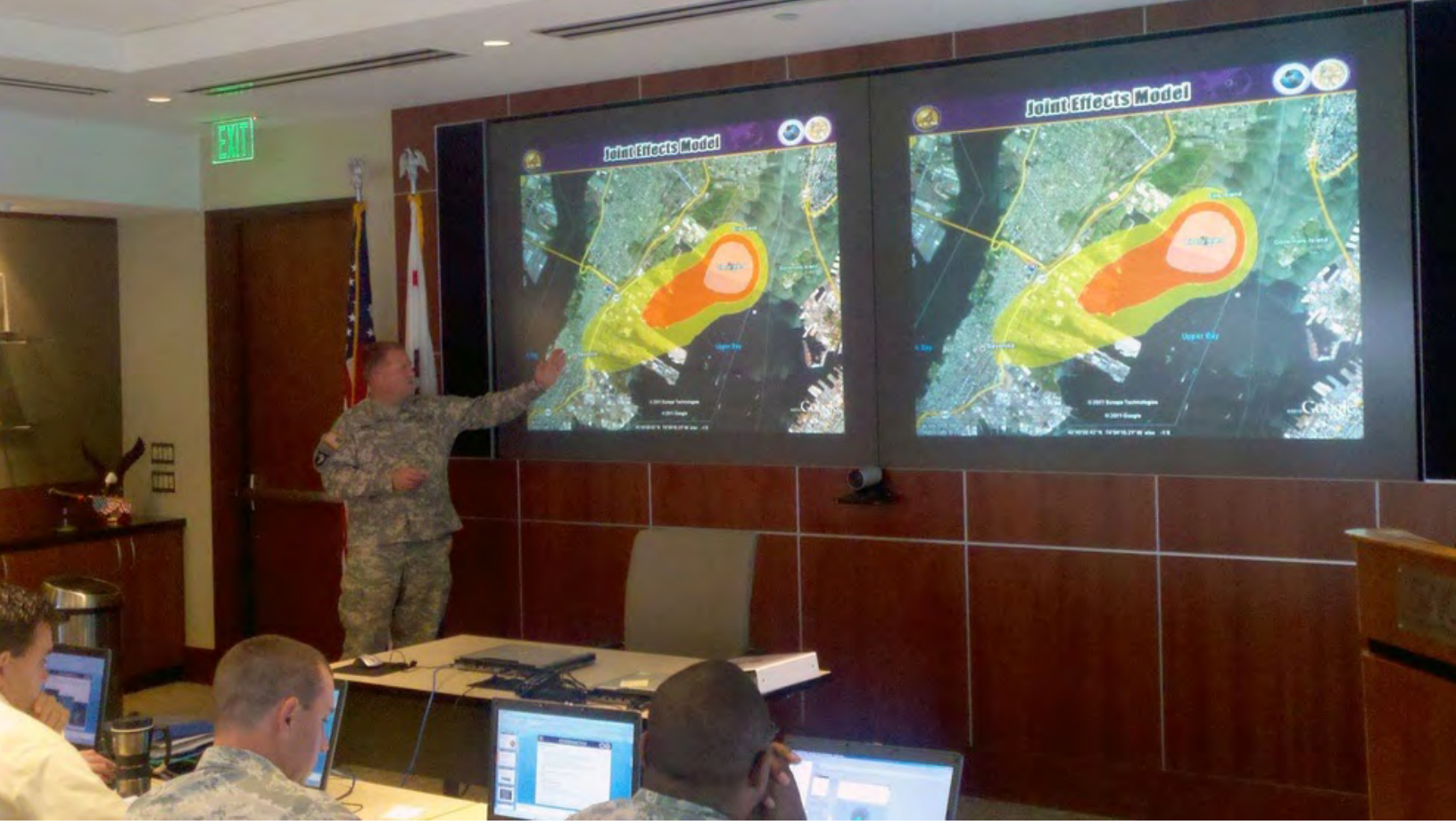
351 Armed Forces Health Surveillance Branch, "DoD Establishes Collaborative Virus Genetic Sequencing Capability for COVID-19," *Health.mil*, June 5, 2020.

352 For specific examples see: Defense Threat Reduction Agency, Joint Science and Technology Office, "All in One Breath," *JSTO in the News*, Vol. 11 No. 6, July 2021; Defense Threat Reduction Agency, Joint Science and Technology Office, "Simple. Sensitive. Specific," *JSTO in the News*, Vol. 11 No. 7, August 2021; Defense Threat Reduction Agency, Chemical and Biological Technologies Department, "Assessing Biohazards Lurking in the Air,"October 10, 2021; John Joyce, "Junior Navy Scientists and Engineers Make Early Warning CBR Detection via UAVs a Reality," Naval Surface Warfare Center Dahlgren Division, June 22, 2017. Defense Threat Reduction Agency's Chemical and Biological Technologies Department, "Be Prepared: Machine Learning is Equipping Us for the Unknown," January 12, 2021.

353 National Academies of Sciences, Engineering, and Medicine, "Biodefense in the Age of Synthetic Biology," 2018: pp. 98-100.



The Joint Effects Model, DOD's primary web-based system for modeling the effects of CBRN weapon strikes and toxic incidents, shows the areas of contamination in colored graphics, not unlike what JPEO-CBRND hopes to do in its experiments. Reporting and tracking, using integrated software solutions, are key to providing coordinated early warning. Joint Project Manager for Information Systems/Department of Defense

Additionally, biodefense organizations have to account for the broadest possible range of biological threats in their pursuit of pathogen early warning. This includes endemic diseases that personnel working in different environments worldwide may be more likely to encounter. Among naturally-arising diseases, those who wish to weaponize pathogens can choose from an immense catalogue of options so long as they can gain access to the right starter strains. For example, they could select pathogens for which detection methods are weakest.[354] Biodefenses must also account for the potential of engineered biological threats, whether deliberately used or accidentally transmitted. This is not unprecedented: the Soviet Union worked to engineer pathogens to evade U.S. standard diagnostic tests.[355]

Given this range of potential threat agents, the United States needs tools that can detect as many pathogen threats as possible, whether known or unknown. Ideally, at least some forthcoming tools will be fully pathogen agnostic. Luckily, the United States and others are already moving in this direction and many relevant technologies are being advanced and deployed today.

Capabilities to detect *any* pathogens have long been an aim of the Department of Defense, and this goal should continue. This serves the interrelated aims of deterrence against biological weapons and early warning for force health and readiness. In one example, two DoD organizations, the Defense Advanced Research Projects Agency (DARPA)

354 Editorial Staff, "Microbiology by Numbers," *Nature Reviews Microbiology* Vol. 9, 2011: p. 628 and Cheri M. Ackerman, Cameron Myhrvold, Sri Gowtham Thakku, Catherine A. Freije, Hayden C. Metsky, David K. Yang, H. Ye Simon, et al., "Massively Multiplexed Nucleic Acid Detection with Cas13," *Nature* Vol. 582, No. 7811, 2020: pp. 277-282.

355 U.S. Congress - House Foreign Affairs Committee, "The Biological Weapons Program of the Soviet Union," testimony by Milton Leitenberg (Washington, DC: 2014).

and the Chemical and Biological Defense Program (CBDP) are funding developments for using CRISPR gene-editing technology as a means to detect all known pathogens at once, a significant improvement over tests today that are most commonly targeted at a single pathogen or—at most—panels that test for a dozen or so.[356] Once a novel pathogen is identified, CRISPR operators can quickly reconfigure the test for new biological threats.[357]

In addition to exploring how to leverage CRISPR's versatility for detection, DoD is examining CRISPR's application as a diagnostic for targeted use after a biological threat is identified in a specific location. In addition to the ability to reconfigure tests quickly, these tools are relatively easy to manufacture and have the potential to be simple to use.[358] DARPA has a program called Nucleic-acids On-Demand Worldwide that seeks to put similar platform technology into a mobile shipping container.[359] An early step in leveraging this development work, once it reaches the right readiness levels, will be to deploy and test its use as a steady-state tool for readiness and deterrence at military bases for which the United States is concerned about the potential use of biological weapons.

Such advances in diagnostic tools can help revolutionize early warning for biodefense. Another early warning data source of emerging importance is advances in materials and sensing capabilities of items defense personnel wear or carry, though the richness of data from such sources is not yet as robust.

DoD has been experimenting with smart devices such as Apple Watches, Garmin Devices, and Oura Rings as a means of detecting pathogens based on the response of the pathogen's host (those who are infected), including increased heart rate, skin temperature, and other factors.[360] The human body necessarily reacts to invading pathogens, regardless of whether they have been previously identified. As such, this approach has the potential to aid as an early indicator of a potentially-concerning pathogen before symptoms are clear.[361] Beyond such basic indicators, host-based detection that moves beyond wearables to materials that sense the body's other reactions to invading pathogens are an interesting area for further research, especially with a focus on the immune system.[362]

Numerous advancements in early warning for biodefense over the coming years will likely stem from genetic sequencing, in particular next generation sequencing (NGS) and metagenomics. By continuing to increase the sophistication by which these approaches are used for reading genetic material, they will likely become as crucial for early warning of deliberate biological threats as they have become for tracking COVID-19 variants.

There are many examples of progress from next generation sequencing. Companies such as IDbyDNA and Karius have shown how this approach can be applied to accurately test for hundreds of pathogens at once.[363] DoD labs have also used NGS for retroactive analyses (e.g., more deeply understanding the risks of pathogens or variants that have already emerged) to inform early warning.

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356 U.S. Department of Defense, Defense Advanced Research Projects Agency, "Detect It with Gene Editing Technologies (DIGET)," 2021; "Sherlock Biosciences Awarded Contract from U.S. Defense Threat Reduction Agency to Support the Development of Ultra-Fast, Ultra-Sensitive Diagnostics," *Sherlock Biosciences*, 2021.

357 James P. Broughton, Xianding Deng, Guixia Yu, Clare L. Fasching, Venice Servellita, Jasmeet Singh, Xin Miao, et al., "CRISPR–Cas12-Based Detection of SARS-CoV-2," *Nature Biotechnology* Vol. 38, No. 7, 2020: pp. 870-874.

358 Ibid.

359 U.S. Department of Defense, Defense Advanced Research Projects Agency, "Nucleic Acids On-Demand Worldwide (NOW)," 2021.

360 Patrick Tucker, "The U.S. Military's Latest Wearables Can Detect Illness Two Days Before You Get Sick," *Defense One*, 2020.

361 Melissa H. Ross, Brittany L. Zick, and Ephraim L. Tsalik, "Host-Based Diagnostics for Acute Respiratory Infections," *Clinical Therapeutics* Vol. 41, No. 10, 2019: pp. 1923-1938.

362 Ibid.

363 See Robert Schlaberg, Heng Xie, Steven Flygare, Yuying Mei, Hajime Matsuzaki, Mark Yandell, and Erin H. Graf, "Detection of Previously Missed Pathogens in Immunocompromised Children With Pneumonia by a Fully-Validated Next-Generation Sequencing Test," *American Thoracic Society International Conference Abstracts*, 2017 and Deborah Levenson, "Metagenomic Next-Generation Sequencing: Modern Tool for Diagnosing Infectious Diseases," *American Association for Clinical Chemistry*, 2020.

An advanced form of NGS---metagenomic sequencing---has proven to be uniquely powerful in detecting truly novel pathogens. Like all forms of sequence-based detection, metagenomic sequencing identifies pathogens based on their genetic makeup. However, a more involved sequencing process and a more sophisticated software backend allow it to identify novel threats. Today this approach is relatively expensive compared to other technologies that can produce robust data, and it requires high levels of expertise to operate the instruments and conduct the data analysis. Given these dynamics as well as its uniquely early warning power, in the near term metagenomic sequencing may be best fit for targeted, high-risk settings such as specific bases and embassies.[364]

As a proof of concept, American and Cambodian scientists have used a workflow developed by the independent non-profit research center Biohub, supported by the Chan-Zuckerberg Initiative, to identify SARS-CoV-2 in Cambodia. The scientists involved simulated having no prior knowledge of the virus and they identified it using similarities with coronavirus pathogens known as of September 2019.[365] Microsoft Research is also innovating in sample collection and processing by using robotics to conduct metagenomic sequencing of insect vectors in specific environments.[366]

Over the past several years, especially during the COVID-19 pandemic, scientists have shown in research papers that the technological solutions described above can revolutionize pathogen early warning. However, it is important to take proofs of concept toward deployment of products at scale. DoD should serve as a testbed for these types of technologies and lead in ensuring they advance in ways that meet biodefense needs as much as possible. DoD appears to be moving in the right direction, connecting scientists and technology developers to end users to facilitate this. For example, the Army Futures Command takes this approach in connecting technical experts from the Combat Capabilities and Development Command with operational experts.[367]

Based on this range of technological advances, **this report recommends a surge in DoD's biosurveillance and early warning investments in the coming years, beginning at $2 billion per year** to leverage the technological advances available that can significantly improve pathogen early warning for biodefense. This will form an important aspect of the nation pursuing a "deterrence by denial" strategy for biological weapons and should help to accelerate early warning for addressing the current pandemic and preventing future ones.

ENSURING INTEROPERABILITY

As early warning for biodefense expands in these directions and others, leaders of relevant programs will need to set guidance to ensure interoperability so that they can contribute to broader early warning initiatives and benefit from them.

When a biological threat is suspected, interoperability enables rapid characterization of the root pathogen, such as how quickly it may spread and the mechanisms for how it spreads. Rapid characterization requires a variety of accessible sources of information. For example, results from mass testing of patients to determine speed of transmissibility and mortality rate, together with genomic information, can help inform laboratory scrutiny of live samples to understand a new pathogen threat.

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364 Jacob Swett, Interview with Authors, May 2021.

365 Katrina L. Kalantar, Tiago Carvalho, Charles FA de Bourcy, Boris Dimitrov, Greg Dingle, Rebecca Egger, Julie Han, et al., "IDseq—An Open Source Cloud-Based Pipeline and Analysis Service for Metagenomic Pathogen Detection And Monitoring," *GigaScience* Vol. 9, No. 10, 2020.

366 "Microsoft Premonition," *The Microsoft Corporation*.

367 U.S. Army, "Team Ignite, Data & Analysis Center Unite Army Research and Concept Communities through Analytics," February 26, 2020.

The AN/TPQ-50 counterbattery radar plays a key part in a JPEO-CBRND experiment at Yuma Proving Ground, providing radar data in which the experiment will look for information on CBRN threats. The experiment's aim is to determine whether radar systems like the AN/TPQ-50 and AN/TPQ-53 can detect ordnance filled with chemical or biological weapons or materiel, either in flight or upon detonation. U.S. Army

Interoperability brings great benefits but is also a challenge due to the range of inputs involved. Integrating new technologies and approaches can be difficult, and so it is imperative to begin guiding investments to ensure they can be combined and used broadly in the years ahead. At a strategic level, the Milken Institute has developed a model of hubs and spokes whereby data from systems all over the world feed into a central hub to allow for analysis for outbreak signals and centralized characterization efforts.[368] This model is in response to one of the key lessons from the pandemic: one country's delaying of sharing information on an outbreak can contribute to cascading failures globally in containment of the biological threat. Having a hub for raw data and to conduct characterization makes time-sensitive information on an outbreak more accessible to countries the outbreak could subsequently spread to. This concept can also be applied between bureaucracies. Pathogens know no borders. Nor do they delineate their spread based on bureaucratic responsibilities. An outbreak can start as an attack on U.S. military personnel and then spread to civilians and vice versa, an argument for a central national and international hub into which biodefense assets are integrated.

Much more work is needed to determine the shape of this moving forward. For the near term, it is imperative that DoD experts work closely with the CDC's Center for Forecasting and Outbreak Analytics regarding interoperability and related issues.

368 Esther Krofah, Carly Gasca, Anna Degarmo, *A Global Early Warning System for Pandemics: Mobilizing Surveillance for Emerging Pathogens*, Milken Institute, 2021.

CONCLUSION

The Council on Strategic Risks maintains a vision of preventing pandemics and deterring interest in biological weapons development and use by convincing malicious actors that these weapons' effects will be nullified by early warning systems, preparedness, and rapid response measures.

More generally, as the global community pursues pathogen early warning in response to the failures of the COVID-19 pandemic, it is essential that natural, accidental, and deliberate threats are all covered, including in ways that meet the biodefense requirements noted above: having pathogen-agnostic capabilities, incorporating tools that can be used in a wide range of use environments, and creating early warning in as timely as a manner as possible, with rich enough data to be useful for active and rapid responses.

The result can be a global pathogen early warning system capable of rapidly detecting and enabling a response to the full spectrum of biological threats, reducing the effects of future outbreaks, regardless of their origin, and decreasing the confidence of malicious actors that biological weapons are worth pursuing.

U.S. Air Force Staff Sgt. James Goeddey, 65th Civil Engineer Squadron Plans and Operations noncommissioned officer in charge, tapes closed a fully-encapsulated hazmat suit worn by Staff Sgt. Samuel Helfrich, 65th CES emergency management technician, during a joint biological response training exercise Sept. 20, 2013, at Lajes Field, Azores. Tech. Sgt. Paul Villanueva II/U.S. Air Force

AN ANNUAL PROGRAM TO EXERCISE & IMPROVE CAPABILITIES

The United States conducts annual exercises for wide-ranging disasters and other contingencies. This has often included exercises to practice responses to infectious diseases striking the American population and agricultural sectors.

The Department of Defense (DoD), the Centers for Disease Control and Prevention (CDC), and other agencies have a strong history of conducting this work with international allies and partners. One of the most important was the Able Response series of biological event response exercises that U.S. and South Korean defense and civilian agencies held from 2012-2015 to improve preparedness.[369]

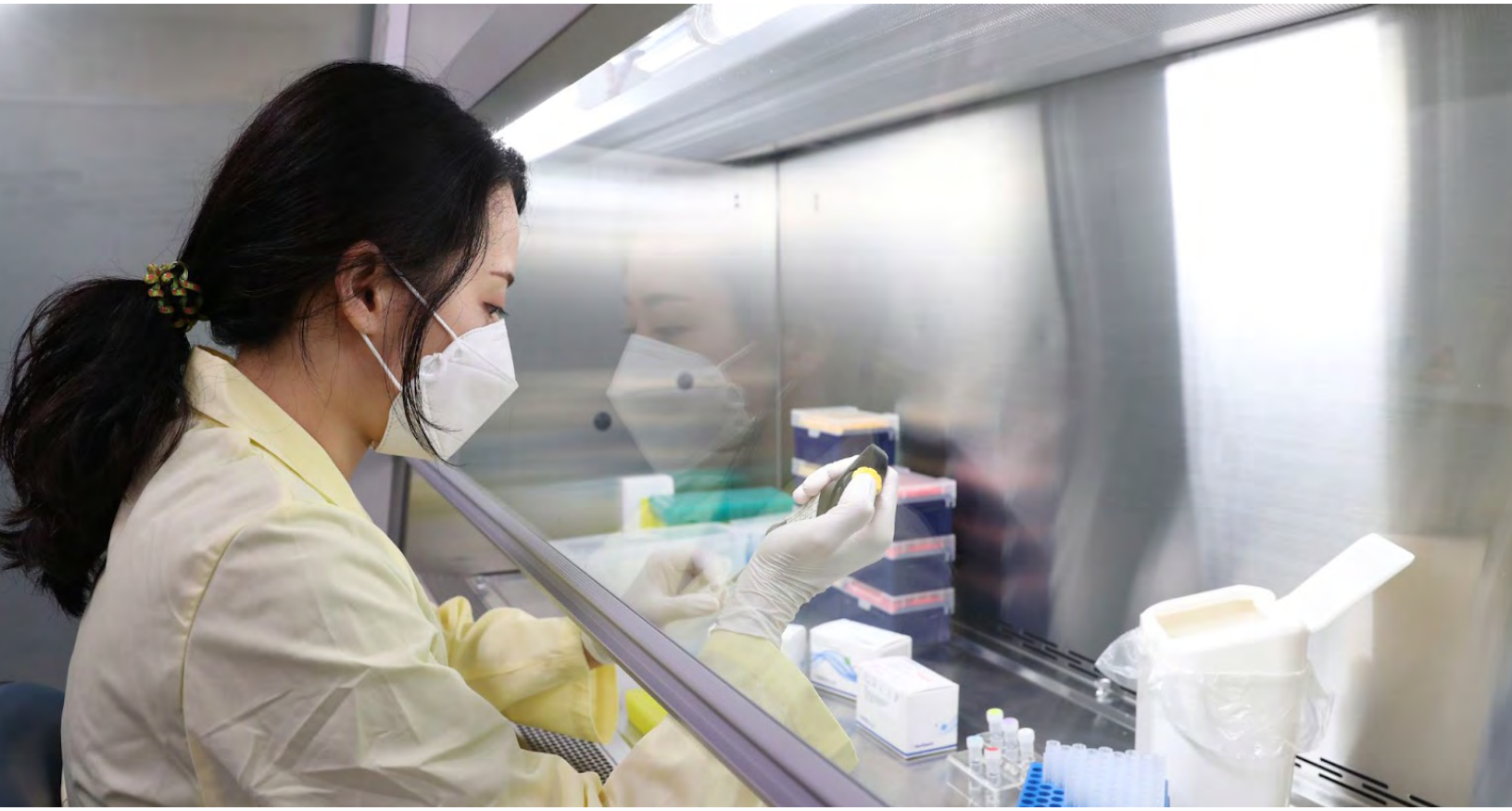
369 Christine Parthemore and Andy Weber, "A Deterrence by Denial Strategy for Addressing Biological Weapons," *War on the Rocks*, 2021.

South Korea (where thousands of U.S. personnel live) has been affected by significant past outbreaks. In terms of biological weapons threats in the region, the U.S. Department of State's annual report on arms control treaty compliance indicates the belief that North Korea is conducting treaty-banned activities (in addition to it not being party to the Biological Weapons Convention).[370] Some unclassified sources regarding operational plans for a conflict with North Korea also posit that, in particular during the early weeks, North Korea may use chemical or biological weapons to deter Japan from entering the conflict, or to demonstrate a willingness to escalate to the use of weapons of mass destruction without crossing the nuclear threshold.

The Able Response exercises helped to enhance preparedness and responses to biological threats to the Korean Peninsula. Over several years, DoD developed new tools for information-sharing, early warning, and responses. South Korean and U.S. personnel from multiple agencies practiced the coordination required for quick and effective decision-making in the event of a crisis. The two nations selected new disease threats to focus on for each year of the exercise to tease out variables that stem from the characteristics of different pathogens.

It is time to replicate and build on these past successes, not least because of the human, economic, and strategic damage COVID-19 has inflicted on the United States and due to rising tensions in Northeast Asia. This should take the form of an annual exercise program to practice and improve early warning of a serious infectious disease threat, rapid development and production of diagnostics and countermeasures, and practice in the data, information-sharing and policy responses needed to respond effectively to a biological weapon.

South Korean company Solgent assembles COVID-19 tests. South Korea was one of the best prepared countries for the COVID-19 pandemic, in part thanks to exercises conducted with the U.S. to prepare for biological threats.
Kim Sun Joo/Republic of Korea



370 U.S. Department of State, *Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments*, 2021: pp. 48 - 49.

The setting for such exercises should alternate annually, but could include different types of military sites—e.g., a large Army base, a Combatant Command (COCOM) headquarters location, a submarine base, or bases outside of the United States. It should also include large civilian population centers that may be likely targets and strategic infrastructure and hubs, such as airports.

The flow of such exercises could look something like the following:

1. A novel pathogen threat is detected and confirmed via daily use of multiple tools. This may include genomic surveillance via next-generation or full metagenomic sequencing, event-based biosurveillance, and advanced environmental monitoring, all of which are in use and advancing in capability today.

2. The detected threat is conveyed to relevant decision-makers. This step would help delineate who needs specific types of information and what decisions they may need to make, including the biosafety containment levels and protocols for handling samples. Other decisions will include when to trigger development and production of diagnostic tests (hopefully very early), whether certain personnel should adopt different behaviors or use additional protections, etc.

3. Developers of diagnostics and medical countermeasures receive genetic sequencing data for the introduced pathogen and begin development. This should become an incredibly fast process, even faster than the new baselines set during the COVID-19 crisis of about two weeks to develop candidates.

4. Various scales of manufacturing are ramped up in different geographies. This will help in persistently understanding supply chain needs and potential bottlenecks that can be worked through in advance. It can also identify where to place future bets to make this process much faster—for example advancing more patch-based, oral, and nasal vaccines that do not require mass supplies of glass tubes, needles, and precision filling and finishing infrastructure.

5. For medical countermeasures, exercises in more quickly conducting trials take place. For candidates of vaccines and therapeutics that have already completed pre-trial testing, these exercises could actually advance them through trials and to FDA clearance as a means of ensuring that past research and development is not wasted, and create countermeasures to more diseases faster. Regarding countermeasures for novel pathogens, this may take the form of a tabletop exercise instead.

6. Practice in distribution and logistics. The U.S. Department of Defense (DoD) and many other entities already exercise and evaluate these systems regularly---and they are already put to the test often. This component of an annual exercise program may therefore focus on how distribution and logistics may be altered as innovations in countermeasure manufacturing and at-home diagnostic testing tools evolve, as these fields may change significantly in the coming years.

This exercise program should be jointly led by the Department of Health and Human Services (HHS) and the DoD, with significant contributions by the Departments of Energy, State, and Homeland Security. This collaboration would not be new; for example, DoD and HHS both played major roles in Able Response, and many government agencies were involved. Actual doses of medical countermeasures produced can be distributed for use across the United States, targeted for use or stockpiling for potentially-targeted military forces, and donated to other nations (including where some diseases are endemic and present high public health threats).

Two overriding goals can drive this work. First, this exercise program should aim to identify ways to halve the time that OWS took to produce COVID-19 vaccines within the next two years. This timeline is ambitious but reasonable—it may even be able to be accelerated further. The Coalition for Epidemic Preparedness Innovations (CEPI) has set forward the goal of developing an effective vaccine within 100 days of the detection of a pandemic threat.[371] This was echoed in the 2021 White House plan "American Pandemic Preparedness: Transforming Our Capabilities," along with related objectives of enabling enough production of the vaccine for the U.S. population within 130 days, and enough for the world in 200 days.[372] In addition, there are several DARPA programs promising to provide a rapid response to pandemics, such as Pandemic Prevention Platform (P3), which seeks to enable production of medical countermeasures within 60 days of threat detection, and Nucleic Acids on Demand (NOW), which aims to enable production of nucleic acid therapeutics and vaccines in just days.[373] Bold goals such as these are key in accelerating the timeline of countermeasure development. Conducting an annual exercise would facilitate the technological and logistical readiness needed to achieve these ends.

Second, this process should be used to bring at least one new medical countermeasure through FDA clearance each year. Some of these can stem from work already completed. Multiple U.S. government agencies have already spent years investing in early-stage research and development for new vaccines and therapeutics, often focused on pathogens of concern as biological weapons threats. Though developing new countermeasure candidates from scratch via platform technologies must be practiced and improved, the United States should leverage past work into products as well.

There are numerous benefits to conducting this work. It can help keep the medical countermeasure ecosystem prepared for emergencies and be used to identify gaps and methods for improvement in advance of the next biological event. These exercises and the relationships formed also have incredible value by directly informing research, development, and acquisition plans to help keep DoD and the nation ahead of biological threats and investing in the most effective and efficient technologies and tools for countering them.

Finally, the United States should extend this annual exercise program to include key allies and partners, perhaps prioritizing those that are contending with high biological weapons concerns.

371 Coalition for Epidemic Preparedness Innovations, "CEPI Launches Plan to Tackle Risk of Future Pandemics and Epidemics," 2021.

372 Executive Office of the President of the United States of America, *American Pandemic Preparedness: Transforming Our Capabilities*, 2021: p. 11

373 Please see United States Department of Defense, Defense Advanced Research Projects Agency, "Pandemic Prevention Platform (P3)," 2020 and United States Department of Defense, Defense Advanced Research Projects Agency, "DARPA Program to Offer Near Immediate Doses of Vaccine, Therapeutics for Infectious Diseases," 2021.

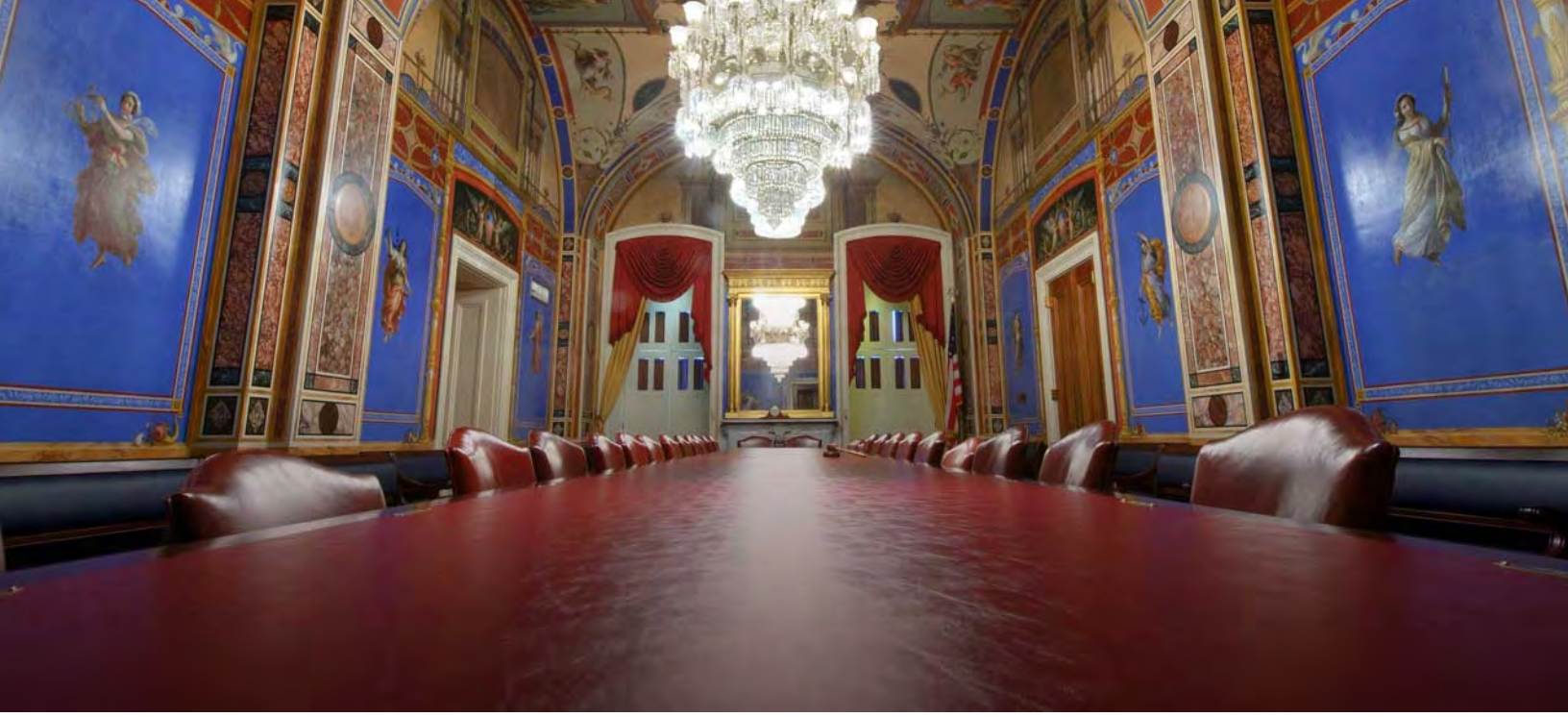
VII. BUDGET RECOMMENDATIONS[374]

As described in this handbook, for the United States to end the mass-destruction threat of biological weapons and prevent future outbreaks from reaching pandemic scales, the nation must make coordinated investments across multiple agencies and functions. Some of the required investments will serve the dual purpose of deterring and defending against deliberate biological threats and preventing future outbreaks of any kind from reaching a pandemic scale. Given that the nation and the world are in a pivotal period in efforts to reduce biological threats, countless government and private sector leaders are beginning to craft a surge in investments to these ends.[375]

The current window is the best possible time for such a surge to be as ambitious as possible. After decades of public and private sector support for innovation paying off, there are more and better opportunities to advance game-changing technologies than ever before---and doing so will support the U.S. economy and national security immensely. Moreover, after the scale of damages to people, economies, and national security caused by the COVID-19 pandemic, delaying significant action may embolden actors who view weaponizing biology as a viable path to strategic advantage.

374 This analysis is based on in-depth research into the U.S. government biodefense enterprise and CSR's own dataset of U.S. government spending on reducing biological threats, drawing on FY10-FY22 budget justification documents for the U.S. government executive branch agencies and departments that contribute to this mission. CSR included programs that counter the full spectrum of biological threats into its analysis. However, in specific, major programs or agencies such as BARDA or Project Bioshield that include work against other threats, CSR estimated annual bio-specific spending based on descriptions within budget justification documents. For example, CSR estimated that approximately 60% of Project Bioshield funding is biological-threat specific (Bioshield also includes spending on chemical, radiological, and other threats), based on a sampling of HHS budget justification documents. CSR is thankful to the Johns Hopkins Center for Health Security for its foundational work on U.S. federal government spending on health security and is building on their efforts to create an updated and more targeted dataset specific to the full spectrum of biological threats.

375 The Biden administration has proposed a $65 billion increase in spending over the next ten years to prevent future pandemics. See the Executive Office of the President, American Pandemic Preparedness: Transforming Our Capabilities, 2021. Additionally, the Bipartisan Commission on Biodefense proposed $100 billion over ten years. See The Bipartisan Commission on Biodefense, The Apollo Program for Biodefense, 2021.



U.S. Congress meeting room for the Senate Appropriations Committee. U.S. Congress

10+10 OVER 10: A MULTI-AGENCY BUDGET ROADMAP

As such, this report recommends that the U.S. federal government adopt a resourcing plan tied to the suggestions presented in this roadmap that we call "10+10 over 10." This entails investments of $10 billion per year (on average) for ten years for deterring and addressing biological weapons threats, plus $10 billion per year for ten years for global health security and direct pandemic prevention initiatives. While this may sound like an astonishing sum, it must be considered in the context of the COVID-19 pandemic alone costing an estimated $16 trillion to the United States in under two years, in addition to the human toll and detriments to national security which are not well quantified.[376] It also represents a small fraction of U.S. government spending overall. Based on CSR's in-depth exploration of this plan with experts in Congress, the Executive Branch, and nongovernmental organizations, we believe this plan to be ambitious but feasible, and certainly high-reward for the nation.

The following tables represent a schematic proposal for the 10+10 over 10 plan, presented in 10-year budgets by agency related to the strategic and programmatic recommendations found in this report.

Table 2 outlines investments specifically applicable to biological weapons threats---for example biodefense and biosecurity programs, Cooperative Threat Reduction partnerships, nonproliferation programs, and robust deployment of the technologies needed to rapidly detect and respond to (and deter) deliberate biological threats. Together they average $10 billion per year over ten years, though this increase over current, insufficient budget levels should ramp up over time.

376 David M. Cutler and Lawrence H. Summers, "The COVID-19 Pandemic and the $16 Trillion Virus," *JAMA* 324, No. 15 (2020): pp. 1495-1496.

TABLE 2: INVESTMENTS IN DETERRING AND ADDRESSING BIOLOGICAL WEAPONS THREATS

	FY2023	FY2024	FY2025	FY2026	FY2027	FY2028	FY2029	FY2030	FY2031	FY2032	*FY2023-32*
Department of Defense	$5,588,000	$6,092,000	$6,597,000	$7,104,000	$7,604,000	$7,854,000	$8,357,500	$8,859,500	$9,359,500	$9,859,500	
Department of Homeland Security	$1,000,000	$1,000,000	$1,000,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000	$1,250,000	
Department of State	$275,000	$275,000	$300,000	$325,000	$325,000	$325,000	$325,000	$325,000	$325,000	$325,000	
Department of Energy	$400,000	$500,000	$550,000	$650,000	$750,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	
Annual Totals	**$7,263,000**	**$7,867,000**	**$8,447,000**	**$9,329,000**	**$9,929,000**	**$10,429,000**	**$10,932,500**	**$11,434,500**	**$11,934,500**	**$12,434,500**	**$100,000,000**

Recommended investments for deterring and addressing biological weapons threats over the next ten years, averaging to $10 billion invested annually. *Note:* For each agency, these funding levels pertain directly to programs and initiatives outlined in this report as critical to addressing biological weapons threats and an effective deterrence by denial strategy. They span biodefense, biosecurity, Cooperative Threat Reduction, nonproliferation, and other such efforts.

Some highlights of this proposal are worth detailing in brief. First, the Department of Defense (DoD) would receive the largest proportion of funding to address biological weapons threats. Because of historical investments, DoD represents one of the nation's greatest concentrations of talent and capabilities to reduce these threats. It has a strong record of successes, many of which are outlined in this handbook. It requires scaling up and adjusting investment strategies to best match the readiness of new and emerging technologies for advancement and deployment in order for the United States to move toward effectively deterring biological weapons and robbing them of catastrophic mass-destruction potential. For instance, the DoD has been one of the few organizations to prioritize approaches that are applicable to addressing and deterring any deliberate biological threat. Its trailblazing in mRNA vaccines, diagnostic tools for rugged environments, and countless other areas have proven that meeting DoD's unique needs in addressing deliberate biological threats provides unrivaled advantages.

The Departments of Energy (DoE), State, and Homeland Security should also see continuing support for resources as part of this roadmap's strategy. DOE and State both would receive significant increases under this plan---as is warranted by both the threats and opportunities at hand.

DoE is primed to leverage its science and technology base to become a world leader in engineering biology, which in itself could be game-changing for staying ahead of biological weapons threats and contributing to deterrence, threat reduction, and preparedness. In particular, DoE's National Laboratories can contribute enormous capability to the nation's efforts. This report recommends that DOE ramp up its bio efforts stepwise over five years, culminating in an approximately $1 billion annual budget into the future, to support this vision and other recommendations outlined in this report.

Likewise, the Department of State's current funding in addressing biological threats is incredibly low compared to the scale of the threat, with bio as just a portion of its approximately $275 million annual countering weapons of mass destruction budget. Ramping up investments to approximately $275 million per year focused specifically on addressing biological weapons risks is warranted, in addition to continuing support for State's other threat reduction and nonproliferation work.

This plan also recommends that the Department of Homeland Security (DHS) receive a steady level of funding for addressing biological threats. As outlined in the DHS chapter above, the department should conduct serious reviews of its current programs and investments. If these reviews point toward the need for (and effective use of) higher levels of funding, that should be considered in the future.

Though noting their multiple benefits, these investments would focus on addressing deliberate biological threats at a high level of ambition: taking biological weapons off the table as a mass-destruction threat. This would complement the second component of the ambitious U.S. strategy recommended in this report: making COVID-19 the last infectious disease outbreak to become a wide-scale pandemic.

Table 3 indicates continuous investments of $10 billion annually over ten years in pandemic prevention and global health security. It shows a recommended increase in Department of State/USAID global health security programs, from around $900 million as reflected in the current President's Budget Request, to $1 billion per year, sustained over time. The increased funding level recommended for the Department of Health and Human Services is a consistent $9 billion per year, with some investments increasing more in the coming years and tapering down over time, and others ramping up over the course of a decade. These variations, detailed in the HHS-focused section below, pertain to technological readiness, ongoing public and private sector investment trends, requirements for post-pandemic resupplying of stockpiles, and other variables.

TABLE 3: INVESTMENTS IN PANDEMIC PREVENTION AND GLOBAL HEALTH SECURITY

	FY2023	FY2024	FY2025	FY2026	FY2027	FY2028	FY2029	FY2030	FY2031	FY2032	*FY2023-32*
Department of State/ USAID Global Health Security	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	
Department of Health and Human Services	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	$9,000,000	
Annual Totals	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$10,000,000**	**$100,000,000**

Recommended investments in pandemic prevention and global health security over the next ten years, summing to $10 billion invested annually. *Note:* These funding levels tie to pandemic prevention and global health security programs and initiatives. They do not incorporate comprehensive public health funding or programs focused on chronic diseases, among others.

As emphasized throughout this report, many of the investments represented across these two summary tables complement and support one another. Many investments aimed at addressing biological weapons threats will aid in pandemic prevention and global health security broadly, and vice versa. Both sets of investments are equally crucial to national security in the 21st century, economic competitiveness, the fostering of a strong bio-industrial base, and saving lives.

The following sections explain the proposed investment levels for the Departments of Defense and Health and Human Services in further detail.

Secretary of Defense Lloyd J. Austin III and Army Gen. Mark A. Milley, chairman of the Joint Chiefs of Staff, appear before the Senate Armed Services Committee in Washington to testify on the fiscal year 2022 defense budget request, June 10, 2021. Chad J. McNeeley/DoD

BUDGET RECOMMENDATIONS FOR THE DEPARTMENT OF DEFENSE

As detailed throughout this report, the Department of Defense (DoD) plays a starring role in addressing biological weapons threats in addition to its contributions to mitigating catastrophic biological threats broadly. The increase in funding this report recommends is a correction to years of de-prioritization of biological threats before COVID-19 and the dramatically reduced budgets that have set back the nation's response capabilities.

These investments are also efficient in that they leverage a strong track record and more than a century of capacity-building within DoD. The Department already has a rational balance of early-stage research and development funding and late-stage funding, driven by its product orientation focused on getting capabilities to military personnel. The biological threat spectrum that DoD has long sought to address is also different and in some ways broader than general public health agencies focus on. As such, it is already investing appropriately in pathogen-agnostic approaches: mRNA platforms, personal protective equipment useful against any and all pathogens, advanced manufacturing and development facilities, detection approaches that are approaching pathogen agnosticism, and more. Finally, DoD's budget is highly transparent, which facilitates both high level guidance from Congress and the Executive Office of the President and public-private cooperation.

TABLE 4: A TEN-YEAR VISION FOR THE DEPARTMENT OF DEFENSE

Department of Defense	FY2023	FY2024	FY2025	FY2026	FY2027	FY2028	FY2029	FY2030	FY2031	FY2032
Chemical and Biological Defense Programs (biodefense programs only)	$2,000,000	$2,500,000	$3,000,000	$3,500,000	$4,000,000	$4,500,000	$5,000,000	$5,500,000	$6,000,000	$6,500,000
Biological Threat Reduction Program	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000
DARPA (biodefense programs only)	$500,000	$500,000	$500,000	$500,000	$500,000	$500,000	$500,000	$325,000	$500,000	$500,000
Health Affairs	$23,000	$25,000	$27,000	$29,000	$29,000	$29,000	$30,000	$32,000	$32,000	$32,000
Department of the Army	$50,000	$50,000	$50,000	$50,000	$50,000	$50,000	$50,000	$50,000	$50,000	$50,000
DoD-wide Early Warning	$2,000,000	$2,000,000	$2,000,000	$2,000,000	$2,000,000	$1,750,000	$1,750,000	$1,750,000	$1,750,000	$1,750,000
Biotechnology	$15,000	$17,000	$20,000	$25,000	$25,000	$25,000	$27,500	$27,500	$27,500	$27,500
Annual Totals	**$5,588,000**	**$6,092,000**	**$6,597,000**	**$7,104,000**	**$7,604,000**	**$7,854,000**	**$8,357,500**	**$8,859,500**	**$9,359,500**	**$9,859,500**

Recommended budgets for bio-relevant DoD programs over the next ten years.

A few highlights within this proposed budget warrant further detail.

First, over the next decade, the DoD should direct the majority of its resources for deterring and addressing biological weapons threats toward the Chemical and Biological Defense Program (CBDP), the primary defense organization responsible for addressing these threats. **This handbook recommends that the next CBDP budget be set to $2 billion, followed by a steady ramp up of $500 million per year to reach $6.5 billion annually over the course of a decade.** This would remain a small fraction of the overall defense budget, yet signal that the United States is taking strong action to reduce its vulnerabilities to biological threats.

This increase in investment is also central to the deterrence by denial strategy we propose, which must extend to CBDP's mission and vision as outlined in *Part V*, *The U.S. Department of Defense* of this report. The CBDP is already investing in approaches that support the mission of deterrence of biological weapons, including in capabilities that are useful against any pathogen threat to help shrink potential U.S. vulnerabilities that adversaries may seek to exploit. Additional funds should accelerate this trend and include the types of investments prioritized in this handbook.

Early on, funding should support a mix of traditional programs and those that are more state of the art. The CBDP is nearing completion of long-running programs to develop medical countermeasures against pathogens that the intelligence community has identified as being particularly likely to be weaponized. With additional funding, the CBDP should push some of these medical countermeasures through FDA approval. The program should also continue its transition to cutting edge approaches to medical countermeasure development that have shown their potential during the pandemic, such as platform technologies and advances in diagnostics. The budget increases we propose would also support the conduct of biodefense exercises as recommended in the DoD section of *Part V* of this report.

The Defense Advanced Research Projects Agency (DARPA) was an early investor in mRNA technology and has consistently performed as a driver of innovation. Aiming toward similarly game-changing technologies, **DARPA's bio investments should expand to approximately $500 million annually** as described in this handbook's *Part V, The U.S. Department of Defense.*

The Biological Threat Reduction Program (BTRP) should also scale up its activities substantially, targeting an annual budget of $1 billion. This reflects the need to prioritize countering biological threats after years of the de-prioritization of this work, as well as the program's expansion to new partner nations and its position as a prime vehicle for deploying U.S. technologies with partners around the world. BTRP should also continue its efforts to improve lab safety, foster strong biosecurity norms, and reduce proliferation risks. As emphasized in this report, if the United States fails to fulfill such needs, this work will be carried out by others, including nations that seek to undermine U.S. security interests.

The DoD Department of Health Affairs and the Department of the Army should maintain investments roughly aligned to current spending, though this may expand in the future if their missions require it, including if organizational changes must be matched with shifting resources.

Next, **this report recommends a substantial and immediate increase in DoD pathogen early warning systems, beginning at $2 billion per year immediately.** This stems from both threat trends and opportunities for significant advancement of U.S. technologies and relevant workforces, as described earlier in the handbook.

DoD has invested in biosurveillance systems for decades as a key part of its approach to addressing biological weapons threats and for force health protection. These investments contributed directly to defense needs in places

such as the Korean Peninsula, and served as a highly productive focus of collaboration with allies and partners. They also helped leap national biosurveillance capabilities forward over that time.

Many technologies to move from biosurveillance, which often lags after biological threats have spread, to true early warning of potentially dangerous pathogens, are now commercially available or nearly so. Across many threat types, DoD takes the approach of moving left of the problem, getting ahead of the worst outcomes and preventing damage to its forces. A large surge of investments now can help accomplish this for biological threats. As shown in the chart above, these investments may be able to taper off over time once robust tools are deployed and personnel trained for their use, when their use enters more of a steady state.

In terms of DoD biotechnology investments, this budget proposal includes a rather modest funding level. This line item mostly reflects DoD's BioIndustrial Manufacturing and Design Ecosystem (BioMADE) industrial innovation center carrying forward as planned, with a slight increase to expand personnel under the Under Secretary for Research and Engineering (e.g., in the form of the Chief Biotechnology Officer role recommended in this handbook, and supporting staff). Such work is important for DoD remaining connected to private sector innovation and vigilant of trends that the department should be leveraging. The modest resourcing recommended for this work reflects the fact that most DoD investments would actually be carried forward under the other programs cited above.

These defense investments, coupled with the aforementioned complementary shifts for the Departments of Energy, State, and Homeland Security, would set the nation on its strongest-ever path toward taking biological weapons off the table as a mass destruction threat. Alongside the work of these agencies, the Department of Health and Human Services is poised to lead significant improvements in preventing future pandemics alongside these and other departments.

U.S. Department of Health and Human Services Secretary Xavier Becerra speaks during a Senate Appropriations Subcommittee hearing in Washington, DC, U.S., on Wednesday, June 9, 2021. SIPA USA/ALAMY LIVE NEWS

BUDGET RECOMMENDATIONS FOR THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Though the Department of Health and Human Services (HHS) is not the sole U.S. agency equipped to prevent future pandemics, it is the most central one. This report recommends an increase to $9 billion per year in investments for HHS programs for innovation in pandemic prevention, health security, addressing biological threats of all sources, disaster preparedness and response, and related functions.

TABLE 5: A TEN-YEAR VISION FOR THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Department of Health and Human Services	FY2023	FY2024	FY2025	FY2026	FY2027	FY2028	FY2029	FY2030	FY2031	FY2032
ASPR - BARDA	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000	$1,230,000
ASPR - Pan Influenza	$320,000	$320,000	$320,000	$320,000	$320,000	$320,000	$320,000	$320,000	$320,000	$320,000
ASPR - BioShield	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000
ASPR - Strategic National Stockpile	$1,100,000	$1,100,000	$1,000,000	$1,000,000	$1,000,000	$900,000	$900,000	$900,000	$900,000	$900,000
NIH/NIAID (select programs)	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000	$2,800,000
ARPA-H (select programs)	$900,000	$900,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000	$1,000,000
Centers for Disease Control and Prevention (select programs)	$1,650,000	$1,650,000	$1,650,000	$1,650,000	$1,650,000	$1,750,000	$1,750,000	$1,750,000	$1,750,000	$1,750,000
Annual Totals	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**	**$9,000,000**

Recommended budgets for bio-relevant HHS programs over the next ten years. *Note:* The increasing investments listed for ASPR in Table 5 reflect increases in the total budget for these programs, of which rising budgets directly relevant to addressing catastrophic biological risks should be a substantial part of the totals. The proposed budgets for NIAID, ARPA-H, and the CDC reflect only these agencies' programs that focus on work that CSR has analyzed as most directly relevant to the vision set forth in this report.

The programmatic changes that these resources would support are outlined in *Part V, The U.S. Department of Health and Human Services* section of this report. This 10-year budget projection represents:

- A substantial increase for BARDA, which continues to accelerate game-changing tools to market.
- An increase in investments for the Strategic National Stockpile over the coming years while it accommodates post-pandemic replenishment and potentially improves stockpiling strategies in the coming years, which may taper off over the next decade (so long as increases are not again warranted due to additional pandemics, disasters, or other major events).
- A steady state of investments for Project BioShield, NIAID, and HHS Pan-Influenza programs.

For ARPA-H, which is newly on the verge of being established as of the publication of this report, the level of investment noted in Table 5 should be dedicated to efforts that focus on emerging infectious diseases and pandemic prevention.

This report also recommends an increase in the CDC's budget for addressing emerging infectious disease threats up to $1.65 billion over the next four years and ramping up to $1.75 billion thereafter. One component of this increase should be significant support for the Center for Forecasting and Outbreak Analytics that the United States stood up in 2021. This recommendation reflects only the areas of the CDC's budget most directly related to infectious disease threats, and it may require a larger overall budget increase for its full set of missions.

Importantly, a stronger budget for HHS is not solely a public health push, though hopefully this would support a paradigm shift in that regard. Improving the nation's ability to address all manner of infectious disease threats is also crucial to effective deterrence against deliberate biological threats and for enhancing the nation's security in countless ways.

OTHER BUDGET RECOMMENDATIONS

This total increase in investments against biological threats to approximately $20 billion a year over ten years is modest in comparison to the costs of inaction. The U.S. government estimates that the annual cost of moderately severe to severe *natural* pandemics is $500 billion-$800 billion just in the United States, calculated based on the projected toll of these pandemics and adjusted based on their likelihood in any given year.[377] Deliberate biological threats are not included in this estimate, meaning the annual price tag of vulnerability to all biological threats could be calculated as much higher, especially if catastrophic-level risks are taken into account. The benefits to the nation's security of using all tools in the U.S. arsenal to mitigate its vulnerabilities to biological threats cannot be overstated.

The balance of funding across agencies that CSR proposes was informed by an in-depth analysis of historical U.S. budgets, alongside more than one year of discussions with experts across government agencies and nongovernmental organizations. The results pointed to several cross-cutting recommendations regarding future budget priorities.

BALANCE AND DIVERSIFY R&D SPENDING

U.S. government research and development spending for new technologies to counter biological threats is concentrated on early-stage research. The result is that the phenomenon of the "valley of death" is more difficult to traverse than in other technology fields. Diagnostics, vaccines, and other medical countermeasures are often developed but abandoned before they can be approved for broad use and procured.

Early-stage research and development is extremely important. However, whether it makes up the largest portion of U.S. government spending on reducing biological threats should depend on the readiness and promise of diverse technologies as well as urgency of filling gaps in national capacities. It should not be taken as a given, and surely there will be times in the nation's future where concentrating more funding toward later-stage development, testing and evaluation, and deployment become urgent.

Moreover, balancing across agencies better will help ensure diversity. NIAID is just one among several organizations conducting early-stage research and development, yet by CSR's estimate it holds around 58% of research and development spending on addressing biological threats. DARPA's budget for reducing biological threats is on average more than eighty times less than NIAID's. But with far fewer resources, DARPA made Operation Warp Speed's success possible with early investments in mRNA technology.[378] Specific programs at organizations such as BARDA and the CBDP's JPEO-CBRND conduct later-stage research and development, and should play a much larger role. Budgets of other organizations that focus on early-stage research should be maintained at a healthy level just as NIAID's budgets have remained so.

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377 Executive Office of the President of the United States, "American Pandemic Preparedness: Transforming Our Capabilities," September 2, 2021. For other estimates see Victoria Fan, Dean T. Jamison, and Lawrence Summers, "The Inclusive Cost of Pandemic Influenza Risk," *NBER Work Pap Series*. 2015: w.22137, p. 24; World Bank, "From Panic and Neglect to Investing in Health Security: Financing Pandemic Preparedness at a National Level," December 2017.

378 Paul Sonne, "How a Secretive Pentagon Agency Seeded the Ground for a Rapid Coronavirus Cure," *Washington Post*, 2020.

INCREASE RESOURCES FOR PATHOGEN-AGNOSTIC APPROACHES

Since the early 2000s, many experts have called for the U.S. government to prioritize programs to develop measures that are pathogen agnostic, i.e., effective against all potential biological threats. The benefits are highlighted by the COVID-19 pandemic, caused by a pathogen with characteristics such as asymptomatic spread that made it particularly difficult to contain. The Department of Defense's CBDP is one enterprise that has moved in this direction with its funding of platform approaches to medical countermeasures starting in the mid-2000s and continually increasing funding for its advanced development and manufacturing facility.[379] More recently, the DoD is investing in detection technologies capable of diagnosing all known pathogens and flagging novel ones.[380]

Over time, advances in pathogen-agnostic tools will allow the further shifting of resources, and they will be critical to addressing deliberate biological threats and novel diseases. For example, CSR estimates that influenza spending alone is around 10% of total U.S. government expenditures on countering biological threats, and this may shift with pan-influenza and even broader disease agnostic approaches. The U.S. government should increase resources in this area, while for the time being continuing to deploy tools that are on hand today (e.g., promising countermeasures and diagnostics that already have FDA clearance or are close to that stage).

Other examples of pathogen-agnostic initiatives and research areas that hold great promise include the following:

- DARPA and CBDP are investing in CRISPR-based diagnostics to help detect all known pathogens.[381]
- BARDA DRIVe is making some of the most forward-thinking investments in the U.S. government, including in means of detecting novel pathogens through the NGS-based Agnostic Diagnostic Program and a program called Beyond the Needle, which is developing innovative means of delivery of any drug, for example through patches.[382]
- DARPA, NIH, and the CBDP have funded nucleic acid-based therapeutics and vaccines that can be reconfigured to counter any pathogen and are easily manufactured.[383]
- DoD and HHS Advanced Development and Manufacturing facilities can be rapidly configured to produce a variety of medical countermeasures, including nucleic-acid-based therapeutics and vaccines. [384]

Overall, these programs currently represent a small fraction of bio spending. This should be increased in the years ahead, which is fully feasible within the funding levels recommended above.

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379 U.S. Department of Defense, Office of the Undersecretary of Defense for Acquisitions, Technology and Logistics, "Transformational Medical Technologies Initiative," (Washington, DC: U.S. Government Publishing Office Publications, 2007).

380 U.S. Department of Defense, Under Secretary of Defense (Comptroller), "DoD Joint Service Chemical & Biological Defense Program Fiscal Year 2021 Program and Budget Review Submission," (Washington, DC, 2020).

381 U.S. Department of Defense, Defense Advanced Research Projects Agency, "Detect It with Gene Editing Technologies (DIGET)," 2021 and U.S. Department of Defense - Chemical and Biological Defense Program, "Department of Defense Fiscal Year (FY) 2021 Budget Estimates," 2020.

382 U.S. Department of Health and Human Services, Office of Biomedical Advanced Research and Development Authority, Division of Research, Innovation & Ventures (DRIVe), "Special Instructions 014 Issuance for Easy Broad Agency Announcement (EZ-BAA) BAA-20-100-SOL-0002," 2021.

383 U.S. Department of Defense, Defense Advanced Research Projects Agency, "Nucleic Acids On-Demand Worldwide," 2021; Douglas Clark, "DARPA, JPEO-CBRND Funds Target COVID-19 Treatment Development," *Homeland Preparedness News*, 2020; and U.S. Department of Health and Human Services, National Institute of Allergy and Infectious Diseases, "Support for Nucleic Acid-Based Approach in Developing Flu Vaccine Platforms," 2020.

384 U.S. Department of Defense, JPEO-CBRND, "Ology Bioservices, Inovio Partner To Manufacture COVID-19 DNA Vaccine With $11.9 Million Department of Defense Grant," 2020.

INCREASE BUDGET TRANSPARENCY

U.S. government spending on reducing biological threats is generally opaque and is becoming more so. The FDA and DHS both made changes in the last few years to combine relevant spending with other activities such as general efforts to counter weapons of mass destruction. It is becoming more difficult to comprehensively track spending to counter biological threats---and this is likely masking even greater cuts to addressing biological threats than the public and policy makers realize.

An exception is DoD, though details regarding its work have been curtailed in recent years as well. One benefit of investments in DoD is that defense authorization bills pass most years, giving Congress certainty, information, and a tool to actively adjust spending on reducing biological threats over time. Making the Chemical and Biological Defense Program's annual report to Congress public would further increase transparency.

At the same time, Congress and Executive Branch agencies must work together to develop budgets and spending reports that more accurately capture and track accomplishments and needs for reducing future biological threats. More transparency will allow oversight committees in Congress and presidential administrations to demand greater accountability of government agencies while also making it easier to direct funding to particularly successful programs.

Congress may also consider innovative authorities that allow smoother pooling of resources across government agencies. Since January 2020, the pandemic has showcased the range of government actors that are needed in case of a pandemic or other biological threat and how they must work together. The HHS and the DoD collaboration for Operation Warp Speed was a case in point.[385]

Any efforts to increase transparency should also help trace how the various agencies contribute to common ends. Executive Branch agencies each have their own strengths and weaknesses in reducing biological threats. For example, BARDA is more product-oriented and managed the development of vaccines and medical countermeasures for COVID-19 alongside an arm of the CBDP responsible for late-stage research and development and also procurement, playing an essential supporting role.[386] Understanding how these agencies and their work are complementary---and equally important----can help diffuse common confusion over whether specific budgets and programs are redundant or reinforcing.

CONCLUSION

The Council on Strategic Risks proposes growing spending on reducing biological threats to $20 billion per year for the foreseeable future. We also have provided guidance on how those funds should be allocated based on lessons from budgets going back over a decade, and research into U.S. government activity to address the full range of biological threats. The current pandemic alone has cost the world trillions of dollars and millions of lives. It is imperative that the nation right-size its responses to biological threats accordingly.

385 U.S. Government Accountability Office, "Operation Warp Speed: Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges," 2021.

386 Please see U.S. Department of Defense, JPEO-CBRND, "The JPEO's COVID-19 Support," 2021 and U.S. Congress, Congressional Research Service, "Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccination Materials," 2021.

VIII. CONCLUSION TO THE HANDBOOK

This *Handbook for Ending Catastrophic Biological Risks* provides a policy roadmap for implementing an ambitious but achievable vision with two interwoven goals: preventing future outbreaks from reaching pandemic scale, and so greatly robbing biological weapons of their intended effects that they are, in effect, rendered obsolete as a weapon of mass destruction. While biological risks will always be present in our world, meeting this vision would effectively end catastrophic-scale biological threats as we know them today.

The Council on Strategic Risks designed this work to maximize its utility for making progress---beginning immediately---in this direction, during a time of significant confusion and uncertainty among the global public regarding how to handle biological risks. As such, the handbook is meant to serve as a clear roadmap for implementing the vision set forth above by breaking down changes that U.S. policymakers should seek for specific organizations, programs, and resources. It also provides numerous examples of specific authorities, leadership actions, and bureaucratic tools that policymakers can leverage to hasten progress in the coming years. In addition to improving its own national policies, the United States must take the lead in promoting this framework to allies and partners, and the international community more broadly.

Pursuing this handbook's recommendations will carry countless benefits. It also offers the strongest path for U.S. security and strategic interests: one that will have immense benefits for economic growth and technological competitiveness. Most importantly, it aims to contribute to a level of preparedness that could save millions of lives by effectively and quickly ending emerging biological threats.

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HOW THE UNITED STATES CAN PREVENT FUTURE PANDEMICS AND DETER BIOLOGICAL WEAPONS

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