JANNE E. NOLAN CENTER
COUNCIL ON STRATEGIC RISKS

DECEMBER 2022

PATHOGEN EARLY WARNING:
A PROGRESS REPORT & PATH FORWARD

Rhys Dubin
Rassin Lababidi
John Moulton
Harshini Mukundan
Lillian Parr
Christine Parthemore
Saskia Popescu
Daniel P. Regan

Edited by Francesco Femia

Pathogen Early Warning: A Progress Report & Path Forward

December 2022

Rhys Dubin, Visiting Fellow, Council on Strategic Risks (CSR)

Dr. **Rassin Lababidi**, Visiting Fellow, CSR

Captain **John Moulton**, USN (Ret.), Senior Fellow, Janne E. Nolan Center on Strategic Weapons (Nolan Center)

Dr. **Harshini Mukundan**, Senior Policy Advisor, CSR

Lillian Parr, Fellow, Nolan Center

Christine Parthemore, Chief Executive Officer, CSR; Director, Nolan Center

Dr. **Saskia Popescu**, Senior Fellow, Nolan Center

Dr. **Daniel P. Regan**, Fellow, Nolan Center

Edited by **Francesco Femia**, Research Director, CSR

Acknowledgements: The authors thank Dr. **Norman Kahn** and the other experts who provided critical insights and feedback throughout the drafting of this report.

Cover photo: Scanning electron micrograph of Crimean-Congo hemorrhagic fever (CCHF) viral particles (yellow) budding from the surface of cultured epithelial cells from a patient. *NIAID*

www.councilonstrategicrisks.org

DESIGN & LAYOUT BY CSR COMMUNICATIONS: ANDREW FACINI & COURTNEY TILLMAN

PRINTED IN THE UNITED STATES OF AMERICA

JANNE E. NOLAN CENTER
COUNCIL ON STRATEGIC RISKS

DECEMBER 2022

PATHOGEN EARLY WARNING: A PROGRESS REPORT & PATH FORWARD

Rhys Dubin

Rassin Lababidi

John Moulton

Harshini Mukundan

Lillian Parr

Christine Parthemore

Saskia Popescu

Daniel P. Regan

Edited by Francesco Femia

Table of Contents

Foreword

By Hon. **Andy Weber**

December 2022

Twenty five years ago, inspired by visionary scientists such as Joshua Lederberg and Roger Breeze, a group of like-minded leaders inside and outside government, of which I was a part, set out to develop a global early warning system that would nip natural epidemics in the bud and deter deliberate biological attacks. We called for a real-time biosurveillance system that would be the functional equivalent of a weather map for infectious diseases.

Thanks in part to the technology acceleration our COVID-19 response unleashed, we are now quite close to achieving such a system. Fast and cheap point of care tests, wearables, sequencing, wastewater surveillance, non-invasive diagnostics, and many other capabilities connected to an information highway will soon reach the point where parents and military commanders alike will know immediately if children or soldiers are becoming sick, and be able to identify the cause even before symptoms manifest. Together with a growing ability to rapidly develop medical countermeasures, such a system can be enacted to deter the development and use of biological weapons by denying mass-casualty or other offensive effects intended by a perpetrator: deterrence by denial of their strategic or operational aims. It will also save millions of lives, and prevent suffering and massive economic losses.

We have called on the U.S. government to launch a **ten plus ten over ten** investment strategy to accelerate and ensure success.[1] That is, an average of $10 billion per year for global health security plus $10 billion annually in biodefense investments for the Department of Defense and other security agencies, each sustained for a decade. This would be among the wisest investments the U.S. government has ever made in this space.

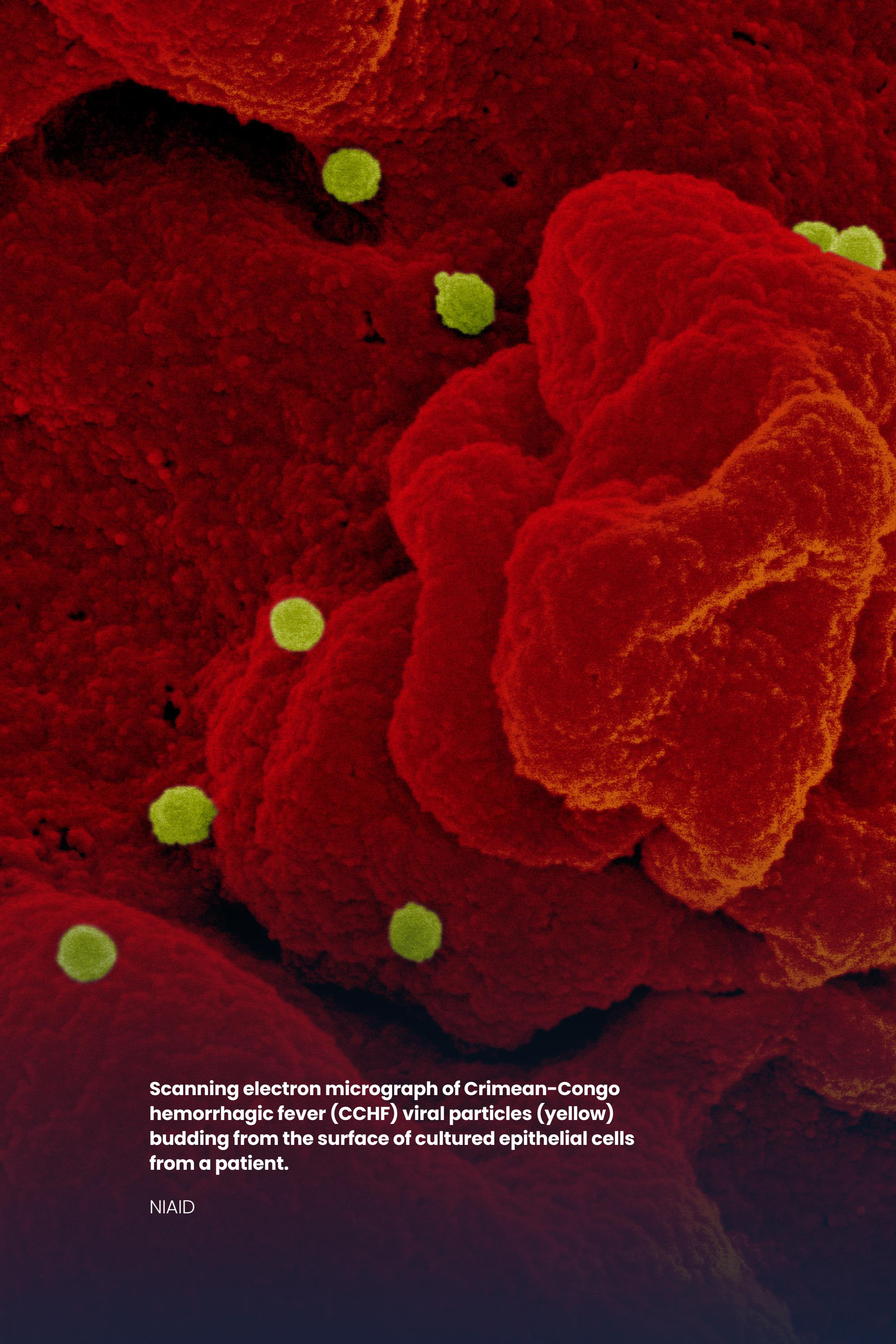
1 Andrew Weber and Yong-Bee Lim, "10 + 10 Over 10: A Funding Vision for the U.S. Fight Against Biological Threats," The Council on Strategic Risks, April 1, 2021.

We should also consider this a starting point for a global surge to achieve pathogen early warning. From a U.S. perspective, this would build on decades of health and biosecurity cooperation with dozens of allies and partners around the world.

Sadly, complacency and COVID-19 fatigue seem to be taking hold in Washington. Currently, the Pentagon spends less than one quarter of one percent of its budget on chemical and biological defense. Congress has been reluctant to embrace the White House's $88 billion "Historic Investment in Biodefense and Pandemic Preparedness," which itself inexplicably had no mention of, or funding for, the Department of Defense.[2]

These investments in public health and biodefense are a national and global security imperative. On top of the devastation of COVID-19 and multiple new outbreaks emerging during the development of this report, Russia's unprovoked invasion of Ukraine has exposed an urgent vulnerability to Putin's potential use of banned biological weapons. For the United States and many other nations, policies are pivoting in the right direction now. However, strategies without major resources are illusions. We urge the U.S. President to include major new funding in the next budget requests, and the new Congress to support them. The world will be a better and safer place if we take bold action.

2 The White House, "FACT SHEET: The Biden Administration's Historic Investment in Pandemic Preparedness and Biodefense in the FY 2023 President's Budget," March 28, 2022.



Scanning electron micrograph of Crimean-Congo hemorrhagic fever (CCHF) viral particles (yellow) budding from the surface of cultured epithelial cells from a patient.

NIAID

Executive Summary

When COVID-19 struck in late 2019 and early 2020, governments worldwide were caught off guard. Despite decades spent improving global capacity to detect, track, and analyze disease threats, the virus still managed to rapidly spread around the globe within weeks. The systems that countries and international institutions established, particularly those designed to spot novel threats before they metastasized into something more dangerous, ultimately proved insufficient to halt COVID-19's spread.

In response to this fundamental challenge, the Council on Strategic Risks (CSR) published an assessment of the state of the global infrastructure designed to alert decision-makers to hazardous pathogens before they touch off significant outbreaks—henceforth referred to as pathogen early warning systems in this report. In July 2021, CSR released the results of this work in our report, *Toward a Global Pathogen Early Warning System: Building on the Landscape of Biosurveillance Today.*[1]

Since then, the importance of effective early warning systems has only increased. COVID-19 has killed more than one million people in the United States alone,[2] and the International Monetary Fund estimates that the global response will cost more than $12 trillion.[3] Scientists are still working to understand SARS-CoV-2's lasting health impacts—ranging from antibiotic-resistant coinfections to a host of other lasting symptoms.[4] Other diseases are also spreading in new and dangerous ways, including monkeypox (now referred to as mpox), a virus once limited to West and Central Africa that has traveled to

---

1 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, July 2021.

2 U.S. CDC, "COVID Data Tracker," accessed November 10, 2022.

3 Andrea Shalal, "IMF sees cost of COVID pandemic rising beyond $12.5 trillion estimate," *Reuters*, January 20, 2022.

4 Ruwandi M. Kariyawasam et al. "Antimicrobial resistance (AMR) in COVID-19 patients: a systematic review and meta-analysis (November 2019–June 2021)," *Antimicrobial Resistance & Infection Control* Vol. 11, No. 45, 2022.

110 countries in less than one year.[5] Ebola has resurfaced in Uganda, spreading to seven districts with infection control measures resulting in school closures.[6] Russia's invasion of Ukraine, moreover, has sparked fears that Moscow might use biological weapons during the conflict.[7]

In light of these developments, this new report aims to update public understanding of contemporary biosurveillance and pathogen early warning capabilities across three dimensions: the United States government, select regions worldwide, and ongoing efforts toward global pathogen early warning integration. This report also seeks to provide an overview of the structural and technical tools required to create effective early warning systems. In doing so, CSR's objective is to provide context for understanding the current state of biosurveillance, while also highlighting notable shifts since 2021. This includes:

- Major U.S. policy rollouts, including the updated National Biodefense Strategy & Implementation Guide, National Security Memorandum 15, the first annual review of the American Pandemic Prevention Plan, and the Department of Defense's (DoD) highly-anticipated inaugural Biodefense Posture Review expected in early 2023.
- The launch of the U.S. Centers for Disease Control and Prevention's (CDC) Center for Forecasting and Outbreak Analytics. The center is actively building its team and capacity as it defines its role in the U.S. pathogen early warning landscape.
- Growing international efforts to bolster effective biosurveillance and early warning capacity throughout Central Asia, Africa, Latin America, East Asia, and the Middle East.

---

5 World Health Organization, "2022 Monkeypox Outbreak: Global Trends," accessed November 10, 2022.

6 Fred Ojambo, "Uganda to Close Schools Early After Children Die from Ebola," *Bloomberg*, November 9, 2022.

7 Gordon Corera, "Russia could launch chemical attack in Ukraine - White House," *BBC News*, March 10, 2022; Robert Petersen, "Fear and Loathing in Moscow: The Russian biological weapons program in 2022," *Bulletin of the Atomic Scientists*, October 5, 2022.

- Increased dialogue by international organizations such as the WHO and the G7 Global Partnership on the future of biological threats and the need for robust global early warning systems.

Despite these examples of progress, however, early warning systems in the United States and around the world remain far from comprehensive. Major structural, technical, and political gaps remain. Namely:

- Biosurveillance capabilities remain largely tied to specific pre-identified threats. Governments and international institutions need to develop a wider set of pathogen-agnostic tools designed to detect any potential novel or deliberate threat.
- Many biosurveillance and early warning efforts lack the resources necessary to be sustainable over the long term. Indeed, some existing capacities may see reduced or halted operations if new funding streams do not arise soon.
- The absence of a standardized approach to assessing the quality of early-warning systems and biosurveillance coverage.
- Within the United States in particular, data sharing and transparency are still insufficient, both across different federal agencies and from state and local public health systems to federal counterparts.
- Although major stakeholders around the world have highlighted the need for comprehensive global early warning systems, no state or international institution has advanced a concrete plan designed to take this challenge on.

Although these gaps are significant, genuine pathogen early warning systems are not out of reach, and many of the necessary digital and technical tools are already available. CSR has therefore laid out a series of recommendations for immediate and near-term action across the U.S. interagency, the global community, and key U.S. partners. These include:

- The U.S. government must establish a clear strategy for the CDC's Center for Forecasting and Outbreak Analytics, including guidance

for how the new center will engage with other agencies across the U.S. government.

- The Department of Defense (DoD) should ensure that its biosurveillance activities and agencies are optimally organized, integrated, and attached to its technology development planning to ensure it provides leaders with timely threat assessments from a variety of sources and evolves ahead of threats.
- DoD should plan and pilot a pathogen-agnostic early-warning system at several strategic military bases and facilities. This could act as a trial-run for a larger national or international system.
- The U.S. government must increase its engagement with the private sector. Companies, including biotech firms, can provide unique data and advanced capabilities that are vital for effective biosurveillance and early warning.
- Governments around the world should prioritize developing interoperable biosurveillance systems. This should lay the groundwork for new cross-border and regional early-warning systems.
- Affluent states should extend existing partnerships and develop new programs designed to bolster biosurveillance efforts in resource-limited and remote settings across the globe.
- Governments and international organizations worldwide should actively pursue a global early-warning framework.

CSR is releasing this report at a critical juncture for national and international biosecurity efforts. Fatigue from COVID-19 and decreasing interest in biological threat reduction pose a real threat to global efforts to address the outbreaks of today and the dangers of tomorrow. Returning to the status quo will not suffice, and experts agree that the drivers and incidence of biological threats will only increase over time.

As an independent nonprofit, CSR will continue its work to support and encourage stakeholders as they consider the guidance offered throughout this report, and help fill the gaps in efforts to chart actionable steps forward. Given how high the stakes are for all actors working to address biological threats, we must continue to push for urgent advancement toward effective pathogen early warning systems.

Scanning electron microscope image of group A *Streptococcus pyogenes* bacteria atop the surface of a neutrophil.

CDC

I. Introduction: Progress Toward Pathogen Early Warning

The COVID-19 pandemic ignited interest in overhauling U.S. and worldwide biosurveillance systems and developing a robust, federated, global pathogen early warning system. Scientists and technologists in the private sector, government, academia, and nonprofit organizations are creating the technological approaches needed to make this vision a reality. If they succeed, such a system will serve as one of the most important tools for stopping an infectious disease outbreak before it becomes a pandemic.

As such, this report seeks to outline some of the major advances in early warning capabilities over the past several years, and highlight open questions regarding how public health, scientific and technology, and defense sectors should collaborate in the future.

In 2021, the Council on Strategic Risks (CSR) produced a high-level assessment of how the biosurveillance landscape has evolved over the past several decades. In the report, *Toward a Global Pathogen Early Warning System: Building on the Landscape of Biosurveillance Today*,[8] we sought to address whether such efforts were close to producing a real early warning system for infectious disease threats: put simply, infrastructure capable of providing timely and sufficiently detailed knowledge of a possible pathogen threat to halt its spread before it creates a significant outbreak, or potentially a devastating pandemic. The same tools could be applied to deterring and, if needed, minimizing the effects of a deliberate biological attack, and/or ensuring that laboratory accidents do not lead to major public health threats.

8 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, July 2021.

Throughout this report, we use the term *biosurveillance* for the processes used to gather, integrate, interpret, and communicate indicators related to biological threats affecting human, animal, plant, and environmental health, as established in the National Biodefense Strategy and Implementing Guide.[9] Yet the changing landscape of biological risks requires getting ahead of the curve, and technological capabilities are emerging that might provide *early warning* of potentially-dangerous pathogens. Many experts around the world are working to understand how to create a global early warning system that takes biosurveillance to the next level: improving the richness of the information provided from biosurveillance activities and the speed with which it is conveyed, and attaching such information to decision processes—all to drive more rapid and effective responses than ever before and mitigate disease impacts. While biosurveillance has advanced over the past 20 years, early warning is required for preventing outbreaks from growing to pandemic scale (not just responding to pandemics) and navigating the reality that accidents and deliberate biological threats may include novel or uncommon pathogens, and ones that onset rapidly.

The results of CSR's 2021 analysis were emblematic of what people around the world were witnessing: a mix of strong but insufficient progress.

During the COVID-19 pandemic, numerous countries, international organizations, and other actors have made swift advances in deploying existing and advanced emerging technologies in a drive toward developing more robust early warning systems. Several key entities, including the U.S. Departments of Health and Human Services and Defense, have also reorganized to more quickly advance biosurveillance activities to bolster their pathogen early warning framework.

Yet that progress has been uneven, and it remains far too fragile.

One central problem in the United States and in other countries has been insufficient policymaker support for the increased investments needed to better leverage critical current and emerging technologies.

9 The White House, "National Biodefense Strategy and Implementation Plan," October 2022.

For the United States, another problem is that while COVID-19 responses drove several significant improvements in early warning tools and their applications, the biodefense and biosecurity sectors have significantly lagged after years of budget cuts and neglect.

The waning of this once highly-influential work has resulted in another worrying trend that could set early warning capacity back by years: the decline of international partnership activities that once drove incredible progress in biosurveillance and biosecurity around the world. This has sent a dangerous message to the world regarding preparedness for wide-ranging biological threats.

Luckily, it appears the U.S. government is in the early stages of addressing the challenges of past declines in domestic and international programs—funneling more effort and attention toward these issues. Nevertheless, Washington must now match recent policy improvements (detailed later in this report) with resources, a renewed surge in collaboration with international partners and nongovernmental experts in the United States, and a re-strengthening of the biodefense workforce. Additionally, one of the most important steps forward will be determining how work across relevant U.S. federal agencies and international entities should evolve to achieve early warning.

There are further reasons to ensure strong integration across these sectors as early warning advances. It is a time of heightened suspicions among nations regarding biological threats. As the United States and other nations expand biodefense activities, if that work is not sufficiently linked to non-defense efforts, it could fuel suspicions regarding its peaceful nature. At the same time, early warning work pursued for pandemic prevention must remain sensitive to minimizing security risks. For example, well-intentioned work to find and understand pathogens in nature that have not yet spilled over to humans could increase risks of accidents and the very spillover it seeks to prevent. As the Soviet Union once conducted such work as part of its biological weapons program, such activities could also cause alarm among nations that needs to be minimized to the extent possible in order for the world to collaboratively advance pathogen early warning that benefits everyone.

While this report is primarily written through a U.S. lens, progress must be made in close collaboration with other nations, organizations, and private sector actors around the world. After a brief chapter describing some of the key elements that are helping to create early warning systems, this report will describe progress and gaps within the United States, followed by examples of how early warning is advancing around the world (with special focus on health security and biodefense opportunities).

The need for progress in pathogen early warning is urgent. As of this writing, the world is experiencing its fifth COVID-19 variant of concern and questions are rising as to whether new ones will emerge that evade the protection of existing vaccines and therapeutics.[10] The World Health Organization (WHO) declared mpox[11] a public health emergency of international concern, and the disease spread throughout 109 countries with 77,174 confirmed cases as of November 1, 2022.[12] In September 2022, the New York State Governor issued an Executive order declaring a State Disaster Emergency following a case of poliovirus.[13] A fast-growing outbreak of the Sudan strain of the Ebola virus is ongoing in Uganda,[14] and Russia's invasion of Ukraine and Moscow's rhetoric around the use of weapons of mass destruction has the defense and policy communities concerned about the use of biological weapons.[15]

---

10 World Health Organization, "Tracking SARS-CoV-2 variants," October 24, 2022; Rita Rubin, "COVID-19 Vaccines vs Variants—Determining How Much Immunity Is Enough," March 17, 2021.

11 The World Health Organization declared that they will implement a name change from monkeypox to mpox on November 28, 2022. The name change will be reflected in the updated International Classification of Diseases.

12 World Health Organization, "Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox," July 23, 2022; U.S. CDC, "2022 Monkeypox Outbreak Global Map," October 27, 2022.

13 U.S. Centers for Disease Control and Prevention, "United States confirmed as country with circulating vaccine-derived poliovirus," September 13, 2022.

14 Elias Biryambarema, George Obulutsa, Estelle Shirbon, "Uganda steps up Ebola response as virus infects 109, kills 30," *Reuters*, October 26, 2022.

15 Gordon Corera, "Russia could launch chemical attack in Ukraine - White House," *BBC News,* March 10, 2022; Robert Petersen, "Fear and Loathing in Moscow: The Russian biological weapons program in 2022," *Bulletin of the Atomic Scientists*, October 5, 2022.

These incidents represent just a handful of the ongoing global biological crises—and potentially even more catastrophic ones are looming. Relatively routine infectious disease threats will continue to arise, most likely at an accelerated pace, along with the risk of new pathogens crossing over to humans or evolving in nature in ways that create more devastating outbreaks and possibly wide-scale pandemics. Many countries are expanding work on dangerous pathogens in an attempt to combat these new threats, yet it will take many years to develop stronger governance of this work to ensure its safety and mitigate terrible accidents. At the same time, the geopolitical environment in which biological weapons threats continue to linger is growing more and more dangerous.

This landscape makes it imperative that the United States and the international community work aggressively toward pathogen early warning. Building on decades of progress and the accelerated deployment of ever-more advanced tools during COVID-19, this is an achievable goal, and one that must be prioritized.

Field team of Tanzanian and Swiss researchers testing for gametocytes of the deadly malaria parasite *Plasmodium flaciparum*.

Lorenz Hofer, University of Basel

II. What Could Strong Pathogen Early Warning Look Like?

The last three years have highlighted the need for agile and robust pathogen early warning systems, designed with interconnected biosurveillance efforts to inform effective responses to any biological threats. On a routine basis, pathogen early warning enables decision-makers to anticipate emerging biological threats, then quickly mitigate and contain the problem. The earlier a system detects a biological threat, the faster modelers and infectious disease experts can assess disease pathways and the more time decision-makers have to develop a potential response.

Additionally, many unique risks in specific settings show the need for early warning of potential disease threats, as compared to slower or retrospective monitoring and reporting. This includes laboratories designed for handling especially-dangerous pathogens, where detection and warning of anything out of the ordinary is important for protecting lab personnel and ensuring accidents do not lead to broader outbreaks.

For many different defense and emergency response organizations, for which some risks are unique (e.g., a biological weapon), the need to immediately understand that a biological agent has been introduced and respond accordingly is even more urgent. In such settings, at the onset of an event, early warning is less about understanding the pathways to disease progression and more about triggering use of pre-planned protective equipment, quarantining or movement of personnel, distribution of pre-stocked countermeasures, decontamination, and other responses. Even across such settings, early warning should be tailored for specific, potentially high-consequence risks—for example, the tools used to help protect personnel on a deployed aircraft carrier and those used in a possible future conflict setting such as the Korean

Peninsula should have similar core tool sets along with augmented capabilities based on the user's needs.

In all cases, an effective and durable early warning approach to pathogens must include multiple interrelated components. Technical prowess to collect and analyze data in a timely fashion across a variety of platforms is required, as is the structural flexibility to meet evolving needs.

Throughout this section, we have outlined many such structural and technical components needed for an ideal version of a pathogen early warning. Recognizing that the needs and emphasis of biosurveillance efforts will vary based on the risks different entities will face, this section aims to establish a baseline capability set that can be augmented for tailored needs. The structural components are crucial for fully resourcing and interconnecting the technical biosurveillance efforts in order to rapidly relay the signals from surveillance into effective response efforts.

Structural Components	Technical Components
• Sustained interest and investment from governments and stakeholders • Internal feedback mechanisms to shift resources and efforts as needed • Pipelines for training the future workforce and retaining experts across the pathogen early warning enterprise • Strategic approaches that include pathogen-specific and agnostic efforts, and awareness for epidemiological relevance	• Tools for collecting samples across multiple levels of pathogen exposure and conducting biological agent identification and characterization • Systems for integrating biosurveillance data across multiple surveillance nodes • Computational analysis for informed decision-making • Public health messaging and response communication

Capacity-building efforts must start with an understanding of what experts and decision-makers would need from early warning tools for specific settings and risks. Predetermined thresholds for action are necessary within early

warning systems, which are often based upon epidemiologically relevant aspects, such as the disease, population, and environment. In other settings, such as in a population that may be targeted with a biological weapon or living near high-containment laboratories, detection of any anomaly is even more important, as compared to monitoring for certain thresholds to be reached.

Structural Components

Early warning capabilities are active and being expanded around the world today. As these developments advance, national-level policymakers should ensure that the early warning capabilities that result are designed intelligently—with a clear vision, sense of strategy, and sufficient resources. No technology can compensate for a lack of component integration or whole-of-government coordination, user oversight, or insufficient use.

A foundational component is a sustainably funded research and development enterprise to produce the tools needed to carry out pathogen early warning activities. Sustained funding should be directed towards the biomedical equipment needed to collect and analyze biological samples, as well as the software systems used to synthesize and analyze vast amounts of data into actionable reporting structures. Funding plans should also be designed to drive continually advancing performance of existing technologies, and platforms should be developed that can be easily scaled and adapted to provide operational flexibility.

Governments would also benefit from strategic plans for early warning that ensure focused efforts are meeting the needs and questions of the community and/or agency. Strategies can range from programs designed to be pathogen-specific to reactive efforts that await signals of novel biological threats. Strategic planning looks at what the ultimate goal is and what is necessary to achieve it. Is the early warning system focused on evolution of a novel pathogen such as SARS-CoV-2, with an emphasis on genomic sequencing in high-risk populations? Does it aim to detect potential surges in cases through

sales of over-the-counter medications? Or is it designed to rapidly detect and respond to a potential biological weapon use?

A strategic approach to early warning systems requires setting thresholds for action and playbooks to guide responses tailored to their settings and needs. Specific thresholds should be considered for decision-making trigger points, which include epidemiologically-relevant aspects unique to the environment, population, and disease. For example, many early warning systems start with a disease-specific approach, which can be the presence of a high-consequence disease (Ebola, smallpox, anthrax, etc.) or a rapid influx of more endemic diseases (influenza-like illness, gastrointestinal illness, etc.) that may point to a larger outbreak or single-point exposure. The epidemiological relevance of a disease should be considered in these thresholds, especially the geographic location. The presence of a pathogen like *B. anthracis* (the causative agent of anthrax) on a military base in a country where anthrax is non-endemic in livestock would likely trigger immediate responses, whereas *Y. pestis* (plague) identified in a hunter in the Four Corners region would not cause the same level of response as the disease is endemic in this area, making natural exposures more likely.

Other considerations must include the population and environment. The trigger points for action often include the surveillance population, which can be as specific as a single town or military vessel. An influx of respiratory illness could be devastating for the continuity of operations in a small setting, which may translate to a more sensitive trigger for biosurveillance and syndromic surveillance systems. Ultimately, thresholds for action should take stock of the population being monitored, epidemiological impact and relevance of diseases, and the environments being studied.

A mixture of pathogen-specific and pathogen-agnostic surveillance techniques is often used to optimize threat detection. A targeted approach for detecting certain microorganisms may be sufficient in discrete locations, whereas an all-hazards approach to identify trends prior to disease detection or even novel pathogens will be necessary for select demographics and sentinel surveillance

efforts. Whole genome sequencing and syndromic surveillance are often strategies that utilize pathogen-agnostic approaches in conjunction with targeted biosurveillance to cast a wide net for early warning.

One potential scenario of this approach would be conducting broad sequencing on high-probability infectious disease patients (e.g., those admitted to hospitals with severe respiratory symptoms) to generate pictures of the current infectious diseases circulating where sampled. A similar concept is currently being conducted with outpatient SARS-CoV-2 samples with Walgreens and Aegis Sciences Corporation, who are publishing the data in an online nationwide index to track the spread and emergence of COVID-19 variants.[16] While the gold-standard for an early warning system would be one that can identify known and emerging pathogens, but also capable of identifying novel pathogens, in some cases it will be more practical to build an initial system targeting select pathogens and then enhance it as necessary.

A common approach is an active biosurveillance program that feeds into a digital analytical network. This includes sentinel testing, or strategic testing of samples and/or populations to pick up deviations from baseline biological presence, combined with digital tools to pick up hits from syndromic surveillance databases. Sentinel surveillance should include locations that are international travel hubs, as well as at-risk populations across human, animal, and agricultural populations and environmental samples. In low- and middle-income countries where clinical testing is limited, surveillance of raw sewage could be an important measure to understanding the disease burden and detecting emerging pathogens.

Analysis of global disease patterns is an important supporting element, and one that creates context and information on trends for decision-makers. This work is sometimes carried out by intelligence or global health-focused agencies in order to catch and understand potential infectious disease incidents around the globe early. This knowledge provides a unique context that, when incorporated with information from early warning systems, can enable a faster

16 Walgreens, "Walgreens Launches COVID-19 Index to Advance Rapid Detection of Omicron and Track Variant Activity by State," January 19, 2022.

response time frame to get ahead of traditional indicators like clinical pathologies and hospital capacity.

Making all of this work—and matter—requires collaboration and cross-functional coordination. There are several elements to such integrated early warning systems that call for multi-agency collaboration, and the range of requirements includes:

- A One Health approach that incorporates human, plant, and animal data.
- Tools that help spot zoonotic threats and emergence effectively.
- A multi-layered approach with depth and breadth across platforms to detect known pathogens.
- Pathogen-agnostic technologies that help ensure that novel or engineered biological agents are caught, not just a predefined list of known threats.[17]

Putting this all together requires expertise across bioinformatics, data analytics, epidemiology, public health, virology, and many more skill sets of a cross-disciplinary team. Information and communication is critical between all levels of government, from the local up to the federal and back down. When these foundational bases for global pathogen early warning are tailored to each country's specificities, the information will need to be synthesized and presented by individuals that are able to clearly interpret the data and offer guidance on actionable measures based on the sum of the whole product. A successful early warning system will enable governments and institutions to rapidly identify potential biological threats, detect emerging infectious disease outbreaks, and provide the information needed to effectively mitigate the pathogens at play.

17 Owen P. Leiser et al. "Beyond the List: Bioagent-Agnostic Signatures Could Enable a More Flexible and Resilient Biodefense Posture Than an Approach Based on Priority Agent Lists Alone," *Pathogens* Vol. 10, No. 11, 2021.

Technical components

Based on decades of investments, today a wide range of tailored technologies and methods can be combined to produce the pathogen early warning that the world needs. Similar to the structural components, there are some that may cover both categories or require consideration at multiple stages of developing an early warning system. As such programs are unique to the needs of those developing it, the following technical components may be prioritized differently based upon needs assessments and goals. Components range from sample collection and analysis to data informatics, and reporting platforms to visualize the data. As technologies are continuously evolving—clearly highlighted during the COVID-19 pandemic—the technological aspect of pathogen early warning must be agile and routinely evaluated. The growing threat of infectious diseases and the scale of needs for an early warning system require the continuous development of new tools. As such, the following sections discuss existing technical frameworks and components, but it should be noted that continued improvement and innovation is needed within this field to address the gaps we currently face and those coming down the pipeline. The following examples of such technical components include many that are in use today and emerging as attractive early warning tools, broken down first into how samples are analyzed to detect pathogens followed by the information systems and approaches that can be used.

Biological Sample Analysis

Biomedical samples will always be core inputs driving pathogen early warning. There are a wide range of options for how to analyze these samples and what data are produced from different tools. The detection and diagnostic platforms selected in advancing pathogen early warning should account for several factors. The first is what surveillance is required when deployed and at the point-of-need, and what surveillance is to be conducted at a reference laboratory. Next is the sample throughput, and understanding the amount of testing that will be required on a routine basis. Another consideration is

the timeline for sample collection, sample preparation, time of the diagnostic test run, and analysis of the results. Successful analysis of biological samples depends on the preparation of the sample workflow and logistics just as much as it depends on the specificity and sensitivity of the analytical technique for providing accurate results. Additionally, these systems should cover the spectrum of pathogens in environmental and non-human reservoirs, human populations deemed to be at high risk of pathogen exposure, and surveillance for asymptomatic and suspected infectious disease cases.

Biological sample analysis is primarily conducted during sentinel and case-based surveillance. For sentinel surveillance, the early warning system is routinely testing at-risk populations, critical infrastructure, and reservoirs of disease to catch the presence or uptick in a biological threat before it presents within a clinical setting. Case-based surveillance is just the laboratory testing of suspected infectious diseases that feeds into the syndromic surveillance pipeline. While these two surveillance types are similar, sentinel surveillance in itself will need to be multilayered to catch known, novel, and engineered pathogens on a routine basis.

Table 1: Select Early Warning Capabilities and Their Target Uses

	PCR	Amplicon Sequencing	Target Enrichment Sequencing	Metagenomic Sequencing	CRISPR-based Assays
Capabilities	Detection & quantification of known pathogens	High-throughput sequencing of a specific target pathogen	Hybrid sequencing approach for multiplexed genetic analysis	Sequencing all genetic material in a sample	Detection of 1,000+ target sequences
Target Use	Case and sentinel surveillance for known pathogens	Detection and mutation tracking for known pathogens	Sentinel surveillance and detection for novel variants of known pathogens	Sentinel surveillance and unbiased detection of unknown pathogens	Surveillance for known pathogens and genetic engineering markers

Polymerase chain reaction (PCR) tests became a well-known tool during the COVID-19 pandemic. They are useful for identifying the presence and quantity of known pathogens within a sample. While PCR tests are commonly used for routine laboratory testing to confirm suspected infectious disease cases, the pandemic expanded their uses into wastewater surveillance as well. Over the last three years, PCR tests have been useful at local levels for routine testing of individuals for identification of asymptomatic cases, confirming suspected infections, and surveillance of the presence of airborne and waterborne pathogens. PCR testing is scalable for high-throughput analysis and can be used to analyze single sequences or run multiplexed panels of over 40 targets with run times under 60 minutes.[18] The timeline for the primers and workflow for a new pathogen of interest can take a PCR-based surveillance group up to 6 weeks to be tested at scale. As such, turnaround could be as low as 2 weeks depending on the resources and optimization in place.[19] However, PCR detection is limited in that it doesn't differentiate pathogens that are living and potentially risky for outbreaks from fragments of genetic material that do not indicate such risks.

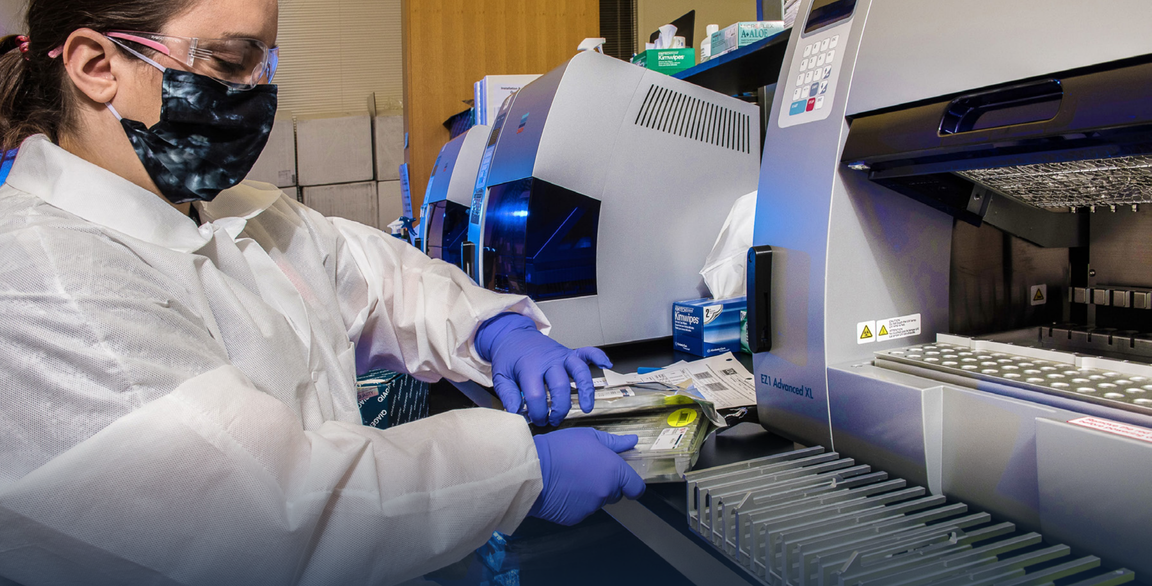
Early warning requires the use of even more advanced tools in addition to PCR. Next-generation sequencing (NGS) tools have been a cornerstone in the characterization of singular pathogens and understanding aspects of the organisms, such as how mutations affect virulence factors contributing to the spread of the disease.[20] Because NGS is detecting the nucleic acids present, NGS is an unbiased detection platform that adds depth to biosurveillance efforts and contributes to early warning.[21] The cost of NGS continues to decrease, an important factor for democratizing the capability set across

18 BioFire, "BioFire FilmArray Panels," accessed November 1, 2022.

19 Author background interview with subject matter expert following Chatham House Rules, October 24, 2022.

20 Martin C. Nwadiugwu, Nelson Monteiro, "Applied genomics for identification of virulent biothreats and for disease outbreak surveillance," *Postgrad Med J*, 2022.

21 Chi-Ching Tsang et al. "Rapid Genomic Diagnosis of Fungal Infections in the Age of Next-Generation Sequencing," *J. Fungi* Vol. 7, No. 8, 2021; Timothy D. Minogue et al. "Next-Generation Sequencing for Biodefense: Biothreat Detection, Forensics, and the Clinic," *Clinical Chemistry* Vol. 65, No. 3, 2018.



This CDC scientist was unpacking testing kits for real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis of SARS-CoV-2 specimens. CDC

regions with different resource levels.[22] Along with the sequencing, NGS requires advanced computational analysis to conduct the bioinformatics required to understand the results.[23] The advancement of computational processing power paired with advancements in computing programming will be important to reduce the total time for analysis and accessibility of NGS platforms as a major component of pathogen early warning.

Within the NGS umbrella are three workflows that contribute different levels of robustness to early warning: amplicon-based assays, target enrichment, and metagenomics (see Table 1 above). These approaches ensure high throughput but also NGS application in both clinical and research settings, allowing for real-world deployment but also research-based efforts. Amplicon-based assays are the least expensive due to their relatively straightforward sample preparation and workflow. Amplicon sequencing is primarily used for targeting specific genetic sequencing of well-established pathogens for high-throughput detection of single nucleotide changes for tracking variants and their characterizations, whereas target enrichment sequencing uses DNA library

---

22 Barton E. Slatko, Andrew F. Garner, Frederick M. Ausubel, "Overview of Next Generation Sequencing Technologies," *Curr Protoc Mol Biol* Vol. 122, No. 1, 2018; National Human Genome Research Institute, "DNA Sequencing Costs: Data," November 1, 2021.

23 Rute Pereira, Jorge Oliveira, Mário Sousa, "Bioinformatics and Computational Tools for Next-Generation Sequencing Analysis in Clinical Genetics," *J Clin Med* Vol. 9, No. 1, 2020.

preparation and hybrid-capture target enrichment to focus on genes of interest. Target enrichment goes beyond the capabilities of amplicon sequencing and is designed to analyze a greater number of genes with better resolution, enabling the detection of novel and emerging variants of known pathogens.[24] While workflow and cost increase for target enrichment, this method of NGS should become more widespread for several reasons; it is well-suited for surveillance of high-consequence pathogens that will be important for advancing capabilities and One Health approaches, and any marginal cost differences are small in context of the high costs of less effective early warning. Critically, the same sequencing platforms used for target enrichment sequencing can be used in stepping up to the use of metagenomic sequencing.

Recently, advancements in the field of metagenomic sequencing have enabled broad-spectrum analysis of the total DNA and RNA present in a biological sample. This provides a technique capable of screening biological samples for unknown, novel, and engineered pathogens.[25] A key aspect of metagenomic sequencing is that it is capable in both laboratory-based systems, and field-able sequencers.[26] This method should be implemented in routine sentinel surveillance of potential reservoirs of pathogens and groups designated as at-risk for novel and/or deliberate biological threats. Analysis of metagenomic sequencing data requires an understanding of bioinformatics and software packages that could limit the implementation of its use in the coming years—for example, the U.S. government should target its expansion to key sites of concern for discovery of novel pathogens, such as international travel hubs and strategic overseas military installations, or biological weapons threats. However, metagenomic sequencing is an important element of sentinel surveillance and part of the pathogen early warning framework for further investigation of suspected novel and/or deliberate biological threats.

24 Illumina, "Targeted Resequencing," accessed December 2, 2022.

25 Bill Beaver et al. "Pathogen Early Warning: New Technologies and Approaches," Council on Strategic Risks, August 21, 2021.

26 Shu Yang et al. "Metagenomic sequencing for detection and identification of the boxwood blight pathogen Calonectria pseudonaviculata," *Sci Rep* Vol. 12, 2022.

Massively multiplexed diagnostics are another core capability that will need to be implemented. These systems are defined by their detection capacity on the scale of 1,000s of target biomarkers per sample. Developments with CRISPR-based detection assays have enabled a new class of detection devices, capable of detecting all human-associated viruses while decreasing the use of biological reagents.[27] These tools will be critical in the analysis of samples probing for all known pathogens, and signatures of bioengineered organisms. CRISPR-based diagnostics have the potential to limit the reliance on some of some key detection elements, such as thermocyclers and biological reagents, broadening the accessibility to resource-limited settings.[28] Relevant biosurveillance entities should incorporate these devices into their capability set for establishing the baseline presence of pathogens and conducting sentinel surveillance, as these devices mature into affordable and fieldable platforms.

One of the critical aspects of biological sample analysis is that the technical capabilities and capacities are rapidly evolving and advancing. CRISPR-based diagnostics are a prime example of a toolset that emerged as a viable platform during the pandemic and is rapidly maturing into robust diagnostic devices. Fieldable devices that combine the low-cost and sample preparation appeal of lab-on-a-chip platforms with the advanced detection capabilities of CRISPR-based diagnostics are currently in development.[29] One example of this is a $9.2 million contract awarded in July 2022 to Georgia Tech Research Corporation for point-of-need detection for pathogens causing sepsis (bacteremia) and respiratory infections as part of DARPA's "Detect It with Gene Editing Technologies" (DIGET) program.[30] Wearable sensors are another technology set that have long been sought to add another tier of data into the early warning pipeline. The use of OURA rings and smartwatches by private industry throughout the pandemic could provide insight needed to integrate data from wearable sensors into artificial intelligence and machine

27 Cheri M. Ackerman et al. "Massively multiplexed nucleic acid detection with Cas13," *Nature* Vol. 582, 2020.

28 Michael M. Kaminski et al. "CRISPR-based diagnostics," *Nature Biomedical Engineering* Vol. 5, 2021.

29 Draper, "Biothreat and Pathogen Detection," accessed November 14, 2021.

30 U.S. Department of Defense, " Contracts for July 15, 2022," July 15, 2022.

learning algorithms for indicators of asymptomatic infection to trigger the next set of testing. These advances in science and technology need continued investment for research and development, especially for studies that focus on end-user applications and integration of these platforms into effective data sources within the early warning landscape. As technology advances into mature diagnostic tools, their incorporation into the early warning pipeline should be considered.

Information Systems & Analysis

In addition to strong advances in the tools needed to analyze samples, detect pathogens, and generate data to characterize them, the methods that can be used to generate knowledge from all that information have evolved in ways that can facilitate early warning like never before. Recent advances in computational technologies, bioinformatics, artificial intelligence, and machine learning capabilities make the ultimate goal of achieving pathogen-agnostic early warning a feasible reality. Indeed, the increased applicability of sequencing and wearable technologies outlined in previous sections is largely due to such advances. In addition, other pathogen-agnostic technologies, such as the collection and curation of spectroscopic signatures for identification of all threat agents, are gaining momentum because of the parallel advancement in machine learning and data integration capabilities.

A scientist in Kenya using new technology provided by the CDC in collaboration with local agencies to assist in disease surveillance.
David Snyder/CDC Foundation

Digital surveillance has advanced significantly to pick up signals that can indicate potential warning signs of an infectious disease outbreak. Advances in machine learning algorithms and computer programming now allow experts to continuously scan open-source information for these indicators. Information produced by local news outlets, social media platforms, transcribed radio broadcasts, and subject matter expert networks can provide signals of potential biological events. Furthermore, information services that collect data on public health and defense unit mobilizations, sudden construction of mobile health clinics and testing centers, and sudden censoring of public communication platforms are important elements to add to pathogen early warning. BlueDot, a global intelligence provider, and ProMED, a community-driven surveillance hub, are two examples of how digital surveillance has been advanced for signaling the potential rise and impact of infectious disease outbreaks over the past decade.[31]

Syndromic surveillance is an approach that has evolved for finding signals of emerging problems faster than waiting hours to days for official diagnosis of patients—for example, noting unusual clusters of symptoms in patients in emergency rooms before their exact diagnoses are completed. Syndromic surveillance systems utilize data from urgent care clinics, emergency departments, and outpatient healthcare

31 Bill Beaver et al. "Pathogen Early Warning: New Technologies and Approaches," Council on Strategic Risks, August 21, 2021.

centers to identify trends in patient symptoms and tests ordered, but can also track over-the-counter medication sales. These systems provide an important capability in tapping large data sets to find disease-associated signals that are used to identify trends of emerging infectious disease outbreaks.

In order for syndromic surveillance systems to be effective, the data upload must provide accurate and frequent updates of records. Often, these systems target emergency department and urgent care center chart fields for chief complaint data of de-identified patient data. Electronic health records, laboratory test results, over-the-counter medical sales, veterinary records, and school absentee data represent some of the key sources that can feed into these systems. Ideally, a robust syndromic surveillance system would capture information of patient demographics, gender, geographic location and timeline of symptom onset through testing collection and results, medical and vaccine history, contacts (human, wildlife, livestock) also exhibiting symptoms, and a common data dictionary.[32]

For example, many existing syndromic surveillance systems like BioSense require not just the technical programs, such as ESSENCE (Electronic Surveillance System for the Early Notification of Community-based Epidemics), for data collection and analysis platforms, but also the integration between electronic health record programs and computational analysis of health information. The capacity to collect the syndromic data from healthcare facilities, such as emergency departments and urgent care clinics, is only the first step in how syndromic surveillance fits into the overarching early warning system and must be followed with effective validation tools, analysis, and a method for translating such data into trends that can be communicated to drive change. The output and effective communication pathway is critical to make the leap from data to decision. In a healthcare setting, this translates to establishing the person and roles responsible for partnering with the local public health BioSense team, internal information technology support, and the roles responsible for monitoring the platform and driving decisions, such as infection prevention, house supervisors, and emergency department leadership.

---

32 Author background interview with subject matter expert following Chatham House Rules, July 20, 2022.

TYPES OF PATHOGEN SURVEILLANCE

The activities that experts around the world count as biosurveillance are highly diverse in terms of how they are conducted and their purpose. All provide valuable input for public health responses and for modeling and forecasting, though approaches vary in how they may contribute specifically to early warning and rapid response. A few common definitions showcase some of these differences.

Indicator-based biosurveillance generally covers structured information reported by health officials and agencies, such as public health agencies reporting the presence of disease cases once patients have presented with symptoms and lab tests have confirmed a diagnosis.

Event-based biosurveillance is a newer set of methods for finding signals in less-organized and more diverse data inputs. According to the CDC, it incorporates "reports, stories, rumors, and other information about health events that could be a serious risk to public health."[33]

Genomic surveillance uses sequencing of a pathogen's genetic code to detect and characterize it, and uses that information in diagnoses and developing medical countermeasures.

Sentinel surveillance stems from networks of doctors, labs, and others voluntarily sharing data on pathogens or trends, which can help reveal patterns of transmission, how diseases affect different populations, pathogens spreading pre-diagnosis, and other information.

***Syndromic surveillance* incorporates** data on specific syndromes provided by (for example) emergency and urgent care centers with the aim of identifying potential outbreaks faster than waiting for official diagnoses of patients.

Vector surveillance is conducted around the world to understand changes in the geographical distribution and density of disease vectors such as mosquitos, including new patterns influenced by climate change.

Note: *This table first appeared in CSR's 2021 report "*Toward a Global Pathogen Early Warning System*" and has been slightly modified.*[34]

---

33 U.S. Centers for Disease Control and Prevention, "Event-based Surveillance," accessed May 25, 2021. See also S. Arunmozhi Balajee et al. "The practice of event-based surveillance: concept and methods," *Global Security: Health, Science and Policy* Vol. 6, No. 1, 2021.

34 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, July 2021.

Systems Integration

The framework of an early warning system mimics the human innate immune system, in that it should be applicable to a wide range of pathogens (if not universal), as well as be easily and rapidly deployable. Thus, a robust and multi-layered early warning system is all-encompassing across the span of biological risks. While every country will tailor its specific early warning strategy to match its resources and needs, this breakdown details several foundational elements that pathogen early warning systems should build upon to be successful in anticipating, detecting, and responding to biological threats. The next step is to ensure that the technical components are properly fed into the pathogen early warning system for analysis and potential investigation of potential biological threats with targeted surveillance efforts.

A well-designed pathogen early warning system will have integration across the surveillance nodes, meaning that a registered detection ping on one surveillance node will cause analysis across the other nodes.

The 2022 outbreak of mpox is an excellent example of how, despite advances, pathogen early warning is not yet a functioning and integrated system.[35] For over 20 years, scientists have warned that mpox had been escalating throughout the endemic regions within Western and Central Africa.[36] However, these warnings did not trigger an effective response from the global community, and on May 7, 2022, the first non-endemic case of mpox was reported in the United Kingdom. By the 18th of May, the first case was reported in the United States. Initially, the approach to pathogen early warning seemed to be a success. A clinician at Massachusetts General Hospital identified a unique disease presentation, referenced the CDC guidance on the report of mpox from the United Kingdom, and alerted the public health system.

---

35 Dan Regan, "100 Days of Monkeypox: Evaluating the U.S. Response to the Emerging Global Outbreak," Council on Strategic Risks, September 12, 2022.

36 Anne W. Rimoin et al. "Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo," *PNAS* Vol. 107, No. 37, 2010; Emmanuel F. Alakunle, Malachy I. Okeke, "Monkeypox virus: a neglected zoonotic pathogen spreads globally," *Nature Reviews Microbiology* Vol. 20, 2022.

However, this is when the systems integration behind pathogen early warning began to break down. Early on, sentinel surveillance efforts to detect mpox were largely not activated, and even those that were activated were not at the scope and scale required to get ahold of mpox in the early days of the outbreak.[37] By 100 days after the first case was identified in the United Kingdom, over 38,000 cases were identified across 90 countries, with 12,636 in the United States.[38] The CDC was already conducting wastewater surveillance for COVID-19, and adding mpox to the workflow should have been a priority for identifying the geographic communities of increased spread to increase sentinel testing for at-risk populations and asymptomatic spread. Mpox was largely misdiagnosed due to the atypical presentation of the disease,[39] and syndromic surveillance efforts and updated guidance should've been improved based on the early reporting from around the globe on the details from the 2022 outbreak. Mpox is a prime example of how individual components of pathogen early warning need to be layered and integrated in a manner that enables feedback across the system to better inform decision-makers and mount an effective response to emerging disease outbreaks.

37 Jennifer B. Nuzzo, Jay K. Varma, "Testing failures helped covid spread. We must do better with monkeypox." *The Washington Post*, June 21, 2022.

38 "Map." Global.health. accessed August 16, 2022.

39 Girometti, Nicolò et al. "Demographic and Clinical Characteristics of Confirmed Human Monkeypox Virus Cases in Individuals Attending a Sexual Health Centre in London, UK: An Observational Analysis." *The Lancet Infectious Diseases* Vol. 22, No. 9, 2022.

THE NATIONAL SECURITY IMPERATIVE OF EARLY WARNING

Increasing the speed and effectiveness of understanding and addressing infectious disease threats is itself a national security imperative. The death toll of COVID-19 on Americans has eclipsed casualties of wars in the past century. This one pandemic has fueled disinformation contributing to new heights of mistrust among nations and publics, inflicted national leaders, affected defense readiness, and cost trillions of dollars.

Early warning of potentially severe emerging disease threats is critical for addressing these risks to U.S. security and stability. It is equally central to preventing accidents from spreading dangerous diseases, including from work conducted in national security laboratories, and to addressing biological weapons threats.

Early warning is required for an effective strategy that includes "deterrence by denial," by which deliberate use of biological weapons would be denied its military or strategic objectives. It is also required for responses that contribute to denial of effects, such as ensuring defense forces can continue operating if biological weapons are used and preventing panic and chaos among civilian populations in affected nations.

A strong incentive for a surge to advance early warning is that actions taken to reduce the effectiveness of biological weapons are largely the same as those used against a naturally occurring pathogen outbreak or an unintentional release from a biological laboratory. This is helpful as the nature of an outbreak may not initially be readily determined or ever known. Early warning work by the Department of Defense for force health protection and deterrence, and by the Department of Health and Human Services or state, local, tribal or territorial public health departments are similar and have similar goals—tailored to unique defense and public health needs depending on the user. In all of these cases involving a replicating pathogen, time is of the essence. Limiting the amount of people exposed and areas where the pathogen could be encountered are both imperative.

Conclusion

While this section has detailed the structural and technical components for successful implementation of pathogen early warning, putting that into practice is another challenge. The ongoing pandemic, ongoing global conflict, and national policy all have a major influence on the form and function of pathogen early warning. In the next chapter, we explore the drivers of pathogen early warning within the United States, and how these efforts can lead to optimized pathogen early warning systems across the whole of government.

Photo of the memorial service held at the National Mall to honor the lives lost to COVID-19 as part of the 59th Presidential Inauguration events.

DOI / Tami Heilemann

III. Early Warning in the United States: Maximizing National Assets

At the time of the COVID-19 outbreak, the United States and numerous countries had many of the essential elements of a pathogen early warning system in place, even if most nations were in the early stages of incorporating more advanced and cutting-edge tools. In the United States, the Centers for Disease Control and Prevention (CDC) and most states were running programs on syndromic surveillance, mechanisms for mandated disease reporting were in practice (albeit patchwork in terms of speed and routine reporting), and countless practitioners were using diagnostic tools including rapid point-of-care tests and genetic sequencing at a considerable scale.

However, critical gaps are lingering. Issues include a lack of coordination between local and federal agencies, vulnerabilities within existing syndromic surveillance systems, and a lack of resources for timely international information-sharing and testing in resource-limited regions.

Early and continuing responses to the COVID-19 pandemic have contributed to filling some of these gaps and building toward stronger early warning capabilities. Advances include the CDC investing in wastewater surveillance and its 2021 formation of the Center for Forecasting and Outbreak Analytics (CFA) to bring more advanced data integration and modeling to the fore. Another important step was the expansion of the Office of the Director of National Intelligence National Counterproliferation Center's mission in March 2022 to now serve "as the lead for the intelligence community for the integration, mission management, and coordination of intelligence activities

pertaining to biosecurity and foreign biological threats, regardless of origin," and renaming it the National Counterproliferation and Biosecurity Center.[40]

While marking significant steps forward, these and other examples have focused significantly on the COVID-19 pandemic and other immediate disease concerns such as the 2022 mpox outbreak and the reemergence of polio. This shows that such advances must not only be sustained, but also expanded in scope to achieve effective, pathogen-agnostic early warning capability.

Such an expansion will require developing an integrated national early warning approach at the same time that U.S. entities are expanding individual capacities—an ambitious objective, but an achievable and crucial one.

This chapter begins with a brief overview of progress made in U.S. policy over the past few years regarding pathogen early warning. We then explore how two of the most central U.S. federal agencies are evolving in terms of early warning—the Department of Health and Human Services (HHS), which includes the CDC, and DoD—with particular focus on how defense and public health activities must come together even as they evolve. The chapter ends by describing the multidimensional ways in which this integration must occur.

40 "§3057 National Counterproliferation and Biosecurity Center," March 15, 2022.

U.S. Policy Progress

Recent updates to U.S. policy tee up a big leap forward when it comes to early warning efforts. Key policy instruction has come through the American Pandemic Preparedness Plan (AP3),[41] National Biodefense Strategy and Implementation Plan,[42] and the National Security Strategy.[43]

In September 2021, the AP3 set a roadmap for building capabilities across the U.S. interagency to improve the federal government's prevention and response to the next deliberate, accidental, or natural biological threat. The AP3 notes that there will be an increased frequency in biological threats for the near future, and acknowledges that the government needs to respond in a more rapid and effective manner than it did during the early COVID-19 response. Included within the five investment areas detailed within AP3 is the call to strengthen pathogen early warning systems. It cements the national objectives of detecting and sequencing pandemic-potential viruses through increased monitoring in clinical and environmental settings, tracking and modeling the spread of emerging pandemics, and modernizing the digital infrastructure required.

One substantial change that AP3 introduced is the shift from listing specific priority pathogens[44] to prioritizing emerging pandemic threats. This will be important for early warning, as such capabilities will be limited if they are designed only to find a specific, limited set of known pathogens. Still, more work can be done in opening this aperture. The AP3 largely uses phrases such as "viral threat," "viral-infection monitoring," and "any virus family" in describing risks. While viruses pose a significant risk,[45] they are not the only biological threats. This is likely a result of the plan being a response to the failures during the

41 The White House, "American Pandemic Preparedness: Transforming Our Capabilities," September 2, 2021.

42 The White House, "National Biodefense Strategy and Implementation Plan," October 18, 2022.

43 The White House, "National Security Strategy," October 12, 2022.

44 National Institute of Allergy and Infectious Diseases, "NIAID Emerging Infectious Diseases/ Pathogens," July 26, 2018.

45 Center for Health Security, "DISEASE X MEDICAL COUNTERMEASURE PROGRAM," accessed November 3, 2022.

COVID-19 response, but it is important to prepare for all high-consequence pathogens, including bacteria, fungi, and multidrug-resistant organisms.

In the first annual report on the AP3's progress, produced in 2022, the White House listed several examples of actions across the interagency that have advanced the goals of AP3.[46] The vast majority of the progress made on advancing early warning systems has been programs that directly address COVID-19. However, many of these capability sets, such as the National Wastewater Surveillance System,[47] can be rapidly augmented to monitor a range of high-consequence pathogens and transition to pathogen agnostic frameworks. The first annual report highlighted that while there has been progress in understanding the spread of the ongoing pandemic, there remains work to be done in preparing for the next high-consequence biological threat.

Separately, the National Biodefense Strategy and Implementation Guide, along with National Security Memorandum 15 (NSM-15) which was issued simultaneously and includes implementation instructions,[48] took further steps forward in mandating real action and resourcing in U.S. efforts to deter and counter biological threats. One of the updated National Biodefense Strategy's biggest advances is elevating focus on deterring biological weapons threats through capacity building, for which advancing early warning will be central.

As part of this capacity building, the strategy aims to further speed up the detection of biological threats and the systems needed to raise awareness of emerging issues, including by bolstering sequencing and data integration across biodefense entities. The ultimate objective is to generate rapid and agile biological threat assessments that can inform responses and recovery efforts.

---

46 White House Steering Committee for Pandemic Innovation, "First Annual Report on Progress Towards Implementation of the American Pandemic Preparedness Plan," September 2022.

47 U.S. Centers for Disease Control and Prevention, "Waterborne Disease & Outbreak Surveillance Reporting," March 21, 2022.

48 The White House, "National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security," October 18, 2022.

Importantly, the strategy acknowledges the interconnectedness of global risks and responses. For example, it sets a goal of improving the biodefense capabilities of at least 50 countries to prevent the spread of accidental or naturally occuring diseases. This line of effort would simultaneously strengthen the international community's ability to deter the development and deliberate use of biological weapons.

The National Biodefense Strategy also reiterates that the nation will address biological threats using a One Health approach that acknowledges the interconnection between animal, human, and plant health.[49] This approach can help policymakers understand and limit zoonotic pathogen spillover, analyze the effects of climate change on previously geographically limited and resurging pathogens, and detect multidrug-resistant organisms. All are crucial for creating a modern pathogen early warning system.

As a complement to the National Biodefense Strategy, NSM-15[50] divides up specific responsibilities across the interagency and identifies biodefense as a national security priority. The memorandum establishes biodefense activities as priorities to be reflected in the annual budgets submitted to the Office of Management and Budget (OMB), and requires the OMB Director to determine if the budget is sufficient to meet the implementation goals of the National Biodefense Strategy. Furthermore, NSM-15 requires additional coordination of biodefense capabilities across the interagency, and requires an annual exercise program, including a White House level Senior Officials Exercise, on biopreparedness, a priority experts have suggested in recent years.[51] Crucially, NSM-15 makes clear that the U.S. government is going to increase the resources and priority given to biodefense capabilities.

49 The White House, "National Biodefense Strategy and Implementation Plan," October 2022.

50 The White House, "National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security," October 18, 2022.

51 William Beaver et al. *A Handbook for Ending Catastrophic Biological Risks*, Council on Strategic Risks, December 2021.

Finally, among other important steps forward, the National Security Strategy issued in 2022 continues to reinforce the Administration's commitment to strengthening national biodefense to address the increasing risk of *catastrophic* biological events both at home and abroad. The strategy includes calls for improvements to pathogen early warning, data sharing, biological threat forecasting, and advancing safe biotechnology development to better address catastrophic-level biological risks. The strategy also increases the prioritization of engagement and transparency with allies and the international community, specifically by strengthening the Biological Weapons Convention and better deterring state and terrorist development and use of biological weapons.[52]

Taken together, these major policy documents indicate that the U.S. government is increasingly prioritizing biodefense and health security generally and early warning specifically. Between the AP3, National Biodefense Strategy, NSM-15, and the National Security Strategy, Washington is beginning to devote the high-level attention necessary to make comprehensive pathogen early warning a reality. Nevertheless, diving into the work of specific agencies, notably HHS and DoD, is necessary to fully understand how implementation is going and examining where improvement is most needed. To this end, the following section outlines agency-specific early warning work before exploring the need for more effective integration across different departments.

52 The White House, "National Security Strategy," October 12, 2022.

The Department of Health and Human Services & Centers for Disease Control and Prevention

In the United States, the strength of public health agencies will continue to play a pivotal role in creating and using pathogen early warning tools to quash outbreaks and prevent pandemics. HHS and the CDC have the ability to collect a great deal of relevant data that can feed into early warning systems. These agencies tie to the local public health entities with key infrastructure, have day-to-day responsibilities, and are important to the initial responses to an outbreak.

As a reflection of hard lessons that have emerged during ongoing COVID-19 responses, leaders in HHS and the CDC have begun experimenting with many changes to their organizing and operations, and investing in innovation through several programs that may hasten the path toward early warning within the United States. This involves ongoing assessment of the current landscape to inform how to move forward.

Biosurveillance Systems within HHS and CDC

Biosurveillance in the United States remains incredibly variable across states, localities, tribal, and territorial systems. As highlighted in CSR's 2021 report, the implementation of biosurveillance capabilities—especially sentinel and syndromic surveillance—is unique in nearly every state.[53]

One of the biggest pushes by the U.S. government to build a system that pooled syndromic surveillance data from across the United States was the adaptation of the software program known as ESSENCE, the Electronic Surveillance System for Early Notification of Community-based Epidemics, into HHS's

53 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, July 2021.

Emergency Operations Center (EOC) at the CDC to assist public health partners in responding to the COVID-19 pandemic. *CDC*

National Syndromic Surveillance Program. The collected healthcare data is integrated through a shared platform, the BioSense Platform, which can be accessed by public health and healthcare partners. The shared access to the BioSense Platform was a result of Congressional mandates in the 2002 Public Health Security and Bioterrorism Preparedness and Response Act. The actual use of ESSENCE, which was originally created by Johns Hopkins University Applied Physics Laboratory and advanced as a biodefense tool by the DoD in 1999,[54] depends on the priorities of the user. For example, Florida's Department of Health has used a modified version of ESSENCE to flag potential indicators of outbreaks like Zika from emergency room chief complaint data,[55] while individual counties throughout Colorado have used ESSENCE to track influenza-like symptoms, suicides, and drug overdoses.

Another source of variability within U.S. biosurveillance is the case surveillance data, rooted in the mandatory reporting of infectious diseases. Each state is responsible for generating the list of infectious diseases that local health departments are mandated to report to the state. However, these lists are based on known diseases and lack the flexibility required to drive timely reporting

54 Howard Burkom et al. "Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE): Overview, Components, and Public Health Applications," *JMIR Public Health Surveill* Vol. 7, No. 6, 2021.

55 U.S. Centers for Disease Control and Prevention, "Florida Department of Health Syndromic Surveillance Identifies Unreported Cases of Zika Virus Disease, 2016–2017," October 20, 2022.

of novel and previously unknown pathogens. This data then flows into the National Notifiable Diseases Surveillance System at the CDC.[56] While this system helps identify novel outbreaks, like the first case of mpox in the United States,[57] the inconsistency in the data depth and timely delivery hampers the ability to ramp up sentinel and syndromic surveillance for emerging outbreaks.

The COVID-19 pandemic highlighted the complex state of integration and feedback across today's biosurveillance efforts within the United States. Many localities and states were performing limited sentinel surveillance and genomic sequencing to further identify infectious disease trends flagged from the case and syndromic surveillance programs. This also included partnerships for airport-based biosurveillance to help monitor flights during the 2021/2022 Omicron surges.[58] COVID-19 started to change the level of sentinel surveillance, with active testing at places of school and work as well as wastewater. Many labs and hospitals ramped up sequencing efforts to better track the distribution and evolution of SARS-CoV-2 variants.

The result is that today, there is more genomic sequencing performed than ever in past, routine biosurveillance activities, as well as advances such as wastewater sampling using both sequencing and PCR-based analysis. This is coupled with more advanced diagnostic tools, increasing use of machine learning, and other tools that are creating a more robust pathogen data and information environment than ever before. All together, this is setting the stage for more advanced early warning than ever before.

56 U.S. Centers for Disease Control and Prevention, "National Notifiable Diseases Surveillance System (NNDSS)," July 20, 2022.

57 Dan Regan, "100 Days of Monkeypox: Evaluating the U.S. Response to the Emerging Global Outbreak," Council on Strategic Risks, September 12, 2022.

58 BioSpace, "Concentric by Ginkgo Confirms Detection of Omicron Variant through COVID-19 Air Travel Biosecurity Collaboration with CDC and XpresCheck," December 7, 2021.

The New CDC Center for Forecasting and Outbreak Analytics

One of the more consequential additions to the government's playbook for early warning is the formation of the Center for Forecasting and Outbreak Analytics (CFA) within the CDC, which was launched on April 19, 2022.[59] COVID-19 put a spotlight on the shortcomings of the government's ability to receive infectious disease data and analyze information for responders. The CFA seeks to fill this gap by developing innovative solutions to use data for disease modeling and forecasting. In this way, the CFA will anticipate and track outbreaks, serving a mission akin to that of the national weather service, but for infectious disease.[60]

The CFA will fulfill three main functions that are crucial to pathogen early warning: infectious disease prediction, briefing policymakers and the public, and innovation within the field of forecasting. As of September 2022, the CFA will be adding at least 40 data scientists to build the forecasting toolbox the CDC needs as it performs data forecasting and modeling and works to translate its work to decision-making. Its current staff is working to take lessons from recent public health emergencies, including on public health communication. Finally, the CFA is designed to continuously innovate—constant efforts to improve data analytics, capture, and visualization will need to remain at the core of its mission.

Before its full launch in the spring of 2022, the leadership team at CFA began modeling the severity and spread of Omicron and provided forecasting information from the federal level down to the local level. This work was analyzed and disseminated to public health officials weeks ahead of the first Omicron disease surges, enabling early preparation for treatments and messaging.[61]

59 Centers for Disease Control and Prevention, "CDC Launches New Center for Forecasting and Outbreak Analytics," April 19, 2022.

60 Caitlin Rivers, Dylan George, "How to Forecast Outbreaks and Pandemics," *Foregin Affairs*, June 29, 2020.

61 Centers for Disease Control and Prevention, "What We Do," June 17, 2022.

A key factor in how successful the CFA will be is its relationships with states, localities, tribes, and territories. This was exemplified during the 2022 mpox outbreak, where the CDC was running a daily telephone operation to receive case and vaccination data from county health systems.[62] The inefficiencies in this system highlighted the need for advancement in data accessibility, standardization, and modernization. Additionally, CFA has recognized the need to increase inclusivity in data collection processes, and is designating roles specifically to engage in historically undercounted and underrepresented populations. This initiative includes community outreach and engagement, especially in regions without internet access. Since its launch, CFA has awarded $26 million in grants to academic and government partners to innovate in forecasting capabilities to support equitable and community-based responses. By capturing data from a wider population, CFA will be better able to detect anomalies and provide early warning for emerging outbreaks.

In addition to enhancing modern and inclusive data collection, the CFA aims to streamline data access and data sharing across the federal public health enterprise by serving as the central hub for synthesizing data streams from tribal, local, state, and federal agencies. This effort alone will not solve all of the barriers currently limiting interagency coordination, but it will serve a critical role in integrating outbreak analytics into a whole-of-government approach. How exactly the CFA helps with integration with DoD in particular, given the widespread defense work described in this report, remains an open question in need of resolution.

The role of the CFA as a single, trusted source of health information during a public health crisis will be crucial for navigating the United States through future outbreaks. Not only will CFA provide more rapid forecasting and analytics than the CDC was historically designed for, but it will also serve to support and benefit from partnerships at the national and local levels to best serve the public. Furthermore, the CFA's mission has been highlighted as a national security imperative in promoting biodefense efforts and health

62 Sanjay Gupta, "Dr. Sanjay Gupta: While monkeypox cases rise, why are we waiting for the cavalry to rescue us?" *CNN*, July 31, 2022.

security, as highlighted in both National Security Memorandum 1[63] and the AP3.[64] CFA's integration with public health and defense agencies will be especially valuable for informing biodefense efforts.

Standing up the CFA was a major step forward, though it must be coupled with other actions. On that front, in August 2022, CDC Director Rochelle Walensky announced a major restructuring of the agency.[65] This will be informed by a recent review of the CDC's pandemic response, and will seek to both modernize the agency and make it more agile for responding to future biological events. Dr. Walensky noted that serious changes need to take place to maximize CDC's ability to respond to future biological events. In particular, she noted that timely data sharing should be a priority going forward—newly detected variants, pathogens, or disease transmission trends should be shared rapidly to enable immediate response. She also focused on the need for more concise messaging, which would allow the public to clearly understand how they could modify their behavior to reduce risk.[66] Messaging is an often undervalued component of early response, and is a crucial component of halting disease spread.

The CDC plays an essential role in both collecting data relevant for early warning, and initiating early response measures. It is critical that the CDC takes the lessons it has learned from the COVID-19 pandemic to ensure better disease control and response in the face of future disease threats.

63 The White House, "National Security Memorandum—1," January 21, 2021.

64 The White House, "American Pandemic Preparedness: Transforming Our Capabilities," September 2, 2021.

65 Lena H. Sun and Dan Diamond, "CDC, Under Fire, Lays Out Plan to Become More Nimble and Accountable," *Washington Post,* August 17, 2022.

66 Krista Mahr, "CDC Director Orders Agency Overhaul, Admitting Flawed Covid-19 Response," *Politico,* August 17, 2022.

New Ventures and Reorganization within HHS

Leadership at the CDC and HHS have also worked to leverage progress made during COVID-19 responses and iron out how responsibilities are shared within the department. This has included both new structures and further organizational changes.

A significant change at HHS came in March 2022, when the Advanced Research Projects Agency for Health (ARPA-H) was launched at the National Institutes of Health (NIH) with a $1 billion budget.[67] The main aim of this agency is 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. ARPA-H is largely modeled after the Defense Advanced Research Projects Agency (DARPA), an agency with a unique structure and a history of conducting innovative, game-changing research. ARPA-H will follow DARPA's funding model: decisions will be made by highly skilled project managers rather than through the traditional peer-review process employed by NIH. Like DARPA, ARPA-H seeks to build a culture that is tolerant of taking risks with high-reward potential.

The Executive Office has also emphasized that ARPA-H will seek to engage with the private sector and build partnerships to bring in new ideas and approaches, as well as to work closely with other agencies in HHS to identify critical needs and to partner on complex issues.[68]

ARPA-H will have a broad focus on health threats, ranging from cancer to infectious diseases. While the exact direction of the agency is not yet clear, the inaugural head of ARPA-H, Dr. Renee Wegrzyn, has been a strong advocate for biosecurity.[69] If ARPA-H is able to recognize the urgency of early

67 Max Kozlov, "Billion-dollar US health agency gets new chief — but its direction remains in limbo," *Nature News,* September 12, 2022.

68 The White House, "President Biden Announces Intent to Appoint Dr. Renee Wegrzyn as Inaugural Director of Advanced Research Projects Agency for Health (ARPA-H)," September 12, 2022.

69 Bryan Walsh, "DARPA changed technology. Now Renee Wegrzyn wants to bring the same innovation to medicine," *Vox,* October 20, 2022.

warning technologies and rapid medical countermeasure development, it has substantial potential to create progress in the early warning and response space. In particular, ARPA-H should commit to conducting innovative, early-stage research on early warning tools (such as pathogen detection technologies) and platform treatment technologies. The high-risk, high-reward culture of ARPA-H may prove valuable in developing early warning technologies that are currently deemed too challenging or likely to fail.

Another major change within HHS came in July 2022, when U.S. Assistant Secretary for Preparedness and Response Dawn O'Connell announced a plan to transition the office from its staff designation to a separate division—newly titled the Administration of Strategic Preparedness and Response (ASPR).[70] As an operational authority, ASPR will now be level with HHS counterparts such as the CDC and the Food and Drug Administration (FDA). This move will allow ASPR to more rapidly respond to national emergencies, such as disease outbreaks, with additional hiring and contracting capacities.

Among other duties, ASPR oversees the Biomedical Advanced Research and Development Authority (BARDA), the Medical Reserve Corps, and the National Disaster Medical System, and manages the Strategic National Stockpile (SNS).[71] Throughout the COVID-19 pandemic, it became clear that ASPR needed more agile ways to surge capacity at BARDA to produce and distribute vaccines and therapeutics. ASPR's elevated role will help drive progress in this direction, making it the lead for working with the industrial base via purchasing contracts to prepare for future infectious disease outbreaks.[72] ASPR's increased capacity and authority may also improve its ability to manage and stock the SNS with Personal Protective Equipment (PPE) and other tools that can rapidly be distributed when an outbreak is detected. Within ASPR, the HHS Coordination Operations and Response

70 Dan Diamond, "Officials Reorganize HHS to Boost Pandemic Response," *Washington Post,* July 20, 2022.

71 Administration for Strategic Preparedness and Response, "About ASPR," accessed November 3, 2022.

72 Sheryl Gay Stolberg and Noah Weiland, "The Biden Administration is Elevating a Division of H.H.S. to More Broadly Oversee Pandemic Responses," *New York Times,* July 20, 2022.

Element (H-CORE) will focus on bringing together public health experts and industry stakeholders to synchronize acquisition and distribution of medical countermeasures.[73] This improved coordination will be a valuable step in avoiding unnecessary regulatory and interagency communication hurdles, serving to streamline outbreak response. H-CORE was established in March 2022 as a permanent entity to sustain the successes of Operation Warp Speed.

Precise details outlining ASPR's elevation have not yet been published, but the move may prove to be a useful step in improving the efficiency of early warning and pandemic response. In particular, ASPR leaders will need to be sure that response activities such as countermeasure development and stockpiling tie to trends in the actionable information produced by early warning systems. Working with other HHS agencies, particularly the CDC, will also be a critical way to foster strong communication and situational awareness for pathogen early warning and detection. Finally, ASPR and BARDA should seek to prepare for currently unknown pandemic potential agents, rather than focusing solely on addressing present threats.

73 Administration for Strategic Preparedness and Response, "H-CORE: HHS Coordination Operations and Response Element," accessed November 3, 2022.

In March of 2020, the COVID-19 outbreak spread throughout the crew of the USS Theodore Roosevelt required the carrier to dock in Guam and coordinate isolation and testing of its crew through its return to sea in June.
U.S. Navy / MC 1st Class Omar Powell

U.S. Department of Defense

The U.S. Department of Defense (DoD) has a long history of leading efforts to address biological risks, including more than a century of leadership in understanding and addressing infectious disease threats. This history ties to the need to protect and treat military forces operating in the tropics and other unique environments, through the emergence of more sophisticated biological and chemical weapons programs during the World Wars and Cold War, and to today's multifaceted, modern range of disease threats that can affect national and international security—potentially catastrophically.

There are countless examples of how DoD's unique missions, reach, and operational authorities have provided significant contributions to the field of pathogen early warning and other innovations in addressing biological risks—and numerous reasons to lean heavily, and proactively, into leveraging this background.

DoD houses organizational frameworks and authorities for transitioning technologies from development to deployment. It has unique requirements for international operations. Across the biosurveillance and early warning landscape, DoD has made significant contributions as both a funding partner and an operational agency. Diplomatic and scientific partnerships through

the Biological Threat Reduction Program (BTRP) provided key global investments that led to the first sequencing of COVID-19 outside of mainland China and millions of samples over the past three years. The Chemical Biological Defense Program (CBDP) drove diagnostic platforms and vaccine development before and during the 2014-2015 Ebola outbreak in West Africa. Funding by the Defense Advanced Research Projects Agency (DARPA) was a key element of the mRNA vaccine platform used in COVID-19.

This handful of examples demonstrates the scope and scale of the impact the DoD can have. The Secretary of Defense has placed an emphasis on continuing this, as the 2022 National Defense Strategy states that DoD will "make the right technology investments," "support the innovation ecosystem, both at home and in expanded partnership with our Allies and partners," and "seed opportunities in biotechnology."[74] Moreover, defense leaders and experts now increasingly understand the national security implications of uncontrolled health threats, and the security gains that can come from its roles in both driving medical research and collaborating with partners around the world on reducing biological risks.

Unfortunately, investment in the U.S. biodefense enterprise was significantly reduced for years—even as the COVID-19 pandemic was ravaging the nation, eventually costing millions of lives and trillions of dollars. CBDP's budget, for instance, has decreased from a high of nearly $2 billion in 2010 to less than $1.5 billion in 2022. CBDP funding for biodefense was particularly hard-hit, dropping from a high of $734 million in 2012 to only $474 million in 2022 (and even decreasing during the pandemic itself, losing nearly $20 million between 2020 and 2022). The Defense Department has also proposed substantial cuts to the BTRP budget, from $225 million in FY21 to $124 million in FY22—a dramatic cut of nearly 45 percent.[75] While Congress has yet to finalize the FY23 budget, DoD's request for CBDP is still under the

74 Secretary of Defense, "National Defense Strategy," October 27, 2022.

75 William Beaver et al. *A Handbook for Ending Catastrophic Biological Risks*, Council on Strategic Risks, December 2021.

FY10 high of $2 billion—and much lower, with a request of $1.3 billion.[76] BTRP is back to FY21 levels, although at just $225 million is insufficient and under-utilizes the program's potential.[77]

This trend is beginning to reverse, as a start to the process of restoring DoD to its historic leadership and ensuring that it can meet its missions. This is long overdue; the deliberate biological threats that drive unique defense requirements are rising, and doing so in a public manner that is ratcheting up tensions among many nations. While the progress being made by the CDC and other agencies are critically important, these agencies will not cover DoD needs and responsibilities in addressing and deterring biological threats. This extends to some of its unique pathogen early warning needs, such as improving it at military bases and on assets like aircraft carriers, and adequately accounting for pathogens that could be weaponized and possibly engineered.

Restoring DoD's role regarding biological risks will require multiple changes, both because of the past years of insufficient investment in this area and because of the ways in which the threat landscape is evolving. As of this writing, it seems clear that many defense leaders understand this and are working to envision the best ways to proceed, including reorganizing how its expansive enterprise conducts biosurveillance given both evolving needs and the emergence of ever more-powerful early warning tools.

Moreover, under the 2022 update to the National Biodefense Strategy, DoD now has more explicit instruction on its roles in this field, including that DoD co-lead the U.S. government's deterrence of biological weapons use along with the Department of State.[78] The White House made further moves in 2022 directing the interagency to prioritize biodefense in its annual budgets and engage the Office of Management and Budget on the implementation of the

---

76 Office of the Under Secretary of Defense (Comptroller), *RDT&E Programs (R-1): Department of Defense Budge Fiscal Year 2023*, April 2022.

77 Office of the Under Secretary of Defense (Comptroller)/Chief Financial Officer, *Defense Operation & Maintenance Overview Book: United States Department of Defense Fiscal Year 2023 Budget Request*, May 2022.

78 The White House, "National Biodefense Strategy and Implementation Plan," October 18, 2022.

National Biodefense Strategy.[79] These directions are critical to ensuring that the biosurveillance efforts are a clear priority in annual budgets, and are adequately resourced to address the systematic approach to pathogen early warning.

Noting DoD's policy mandates to move forward in this direction, this section will highlight some of the major questions and issues related to DoD's ongoing reorganization of its biosurveillance activities and its ongoing work to envision its optimal roles in pathogen early warning. They include how best to develop strong capabilities at U.S. domestic bases, the need to revive international partnerships, and leverage all of DoD's biosurveillance and early warning nodes globally into an integrated, effective systems approach.

Enhance Early Warning on Military Bases in the United States

In the coming years, DoD should launch an initiative to improve pathogen early warning across all its U.S. bases. This will look different across geographies and settings, and should leverage interconnections with area communities in order to deepen the interfaces between defense and broader public capabilities.

First, DoD should aim to quickly develop an ideal, cutting-edge base early warning system at several select bases. These locations should be selected to account for endemic and potentially deliberate disease threats, their importance to continuity of operations and conflict contingencies, and other factors. Efforts at these locations should be seen as test beds for the most cutting-edge tools, such as metagenomics, advanced environmental monitoring equipment, experimental data analytics, and more. The objective should be to quickly achieve greatly improved, disease-agnostic capabilities to the best degree possible. Top candidate locations could be the cluster of bases in Hawaii that include U.S. Indo-Pacific Command headquarters and key sites in the Washington, D.C. region.

79 The White House, "National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security," October 18, 2022.

Second, DoD should simultaneously identify more cost-effective ways to quickly ramp up capacity at all bases, with year by year deployment plans. This could include ensuring that labs on or near bases are using next-generation sequencing and massively multiplexed detection tools, wider-spread use of bioaerosol and wastewater sampling, and integration with wearable devices to layer information from potential reservoirs of disease to the onset of signs and symptoms of infection.

Third, tailored approaches should be designed for locations with unique roles in national incident and emergency responses. For the Department of Defense, this would likely include U.S. Northern Command (NORTHCOM), as part of its homeland defense mission is to detect threats to the United States. While the aerospace and maritime early warning aspects of this detect mission are well understood and executed by the U.S.-Canadian North American Aerospace Defense Command (co-located with NORTHCOM in Colorado Springs), there is not a similar robust capability for biological threats. Besides the U.S. government's desire to avoid human suffering and adverse economic effects that were experienced with COVID-19, NORTHCOM would greatly benefit from having a pathogen early warning system to help maintain the U.S. armed forces' ability to generate and deploy forces from the continental United States and Alaska. Naturally, such an early warning system would be more effective if it was integrated with other federal, state, local and tribal efforts, which dovetails well into NORTHCOM's pursuit of a "globally integrated layered defense." Within this construct, NORTHCOM describes its "homeland defense layer" as having its capabilities "integrated with the whole-of-government/interagency and strategic private sector partner capabilities,"[80] which would also benefit NORTHCOM as the command has few permanently assigned forces.

Each U.S. military service would also play a key role in establishing a pathogen early warning system, as services, not NORTHCOM, have authority over most of the forces and installations in the continental United States, including funding responsibility. To capitalize on success and learn from mistakes,

80 NORAD and NORTHCOM, "Strategy Executive Summary," March 2021.

this pathogen early warning system should start as a series of base-wide pilot projects at select U.S. military bases so that each service can participate in and better understand any service-unique needs or constraints. Also, in conjunction with the pertinent combatant command, pilot projects should be undertaken by the services at several U.S. overseas installations. This overseas effort should also include information sharing with the host-nation, so that transparency can build good will, benefit both countries by establishing a more complete picture, and help limit the susceptibility of these programs to adversary information operations.

Improving the tools used for pathogen early warning at U.S. bases should be seen as part of deterrence, homeland defense, personnel readiness, and biosecurity strategies for the nation. This will be key to early warning triggering rapid and effective responses where infectious disease threats emerge, yet it must also be designed to aggregate and learn from data nationally.

Revive International Partnerships & Programs

Of course, DoD's mission requires significant work around the world. Its work to advance pathogen early warning must extend to its global activities and partnerships.

Though it has waned in recent years, pathogen early warning has always been an important aspect of DoD's activities. Many DoD programs and activities around the world have been on display through the COVID-19 pandemic. The Global Emerging Infections Surveillance (GEIS) program, established in 1997, combines input from U.S.-based defense agencies and defense-related labs internationally. It has been conducting genetic sequencing duties for DoD for years. Leveraging the Next Generation Sequencing and Bioinformatics Consortium and its experience with Ebola and Zika, GEIS began monitoring SARS-CoV-2 transmission among DoD personnel in early 2020. It also compared SARS-CoV-2 sequences to surveillance efforts and bioinformatic data across DoD overseas labs, including Thailand, Peru, Kenya, and Cambodia.[81]

81 Health.mil, "GEIS Partners," accessed November 8, 2022.

U.S. Air Force Maj. Andrew A. Herman and Maj. (Dr.) Godwin B. Bagyenzi, director of medical research for Uganda People's Defense Force Health Services, give a deworming tablet to a villager in Kakute, Uganda. *U.S Navy / PO1 Tom Ouellette*

In many ways, DoD's international reach has been even more extensive through its long-term collaboration and partnerships with other nations. DoD launched its flagship program in this field as part of the Nunn-Lugar Cooperative Threat Reduction (CTR) Program in the wake of the dissolution of the Soviet Union. The CTR Biological Threat Reduction Program (BTRP) has long been used to expand biosurveillance and early warning capacity in key locations around the world. BTRP has partnered with countries across the former Soviet bloc, Southeast Asia, the Middle East, and Africa to bolster their own capacity to anticipate, detect, and respond to infectious disease outbreaks.

Indeed, the BTRP has helped to create a landscape that features nations and regions that are primed to advance global pathogen early warning capacity, as described in Chapter 3. Moreover, though DoD's motivation for this work includes addressing biological weapons threats, the program has consistently advanced both biodefense and public health security, and has driven integration across defense, scientific, and health agencies.

Unfortunately, as described above (and in more detail in CSR's *Handbook for Ending Catastrophic Biological Risks*),[82] DoD has allowed this work to atrophy significantly. This heightens many risks. One is a weakened ability to quickly

82 William Beaver et al. A Handbook for Ending Catastrophic Biological Risks, Council on Strategic Risks, December 2021.

detect significant emerging disease threats—including for countries where DoD's work is ending before additional resources within countries or with other partners are set to fill any gaps. Another is loss of trust in the United States as a strategic partner, and an associated risk that China, Russia, or other adversarial nations will become partners of choice to longtime U.S. collaborators. One of the best ways DoD should contribute to the advancement of early warning is to revive BTRP in general and renew its focus on expanding early warning around the world. This should be done urgently, and with far greater transparency regarding BTRP's plans with other nations around the world.

Additionally, DoD should develop plans to reinvigorate the use of the international Navy Medical Research Units and other DoD overseas labs. These international labs are a permanent presence that pair U.S. personnel with the host nation, building skill sets for both groups and establishing a culture of collaboration. They can also serve as regional hubs for biosurveillance work. Leveraging the Global Emerging Infections Surveillance program at the international labs is essential for establishing a true global pathogen early warning system. The location of these units should be considered for future installations to capture areas where research on infectious diseases can address new variables and threats.

Developing A Systems Approach

After over several decades of improving biosurveillance and early warning tools, today DoD has numerous entities involved in this work within the United States and across the world. One concern within DoD has been that its biosurveillance efforts are not operating in a truly integrated approach. At the same time, DoD and others have driven remarkable progress in developing and deploying new tools for detecting and tracking disease threats, often in ways that go beyond those used for common public health work. This includes the early development of ESSENCE and field deployable diagnostics like the Joint Biological Agent Identification and Diagnostic System.

As these and other factors have evolved, DoD has begun reconsidering how to create an integrated, systems approach to biosurveillance and advance it toward true early warning. While tailored tools and methods are often warranted, they must come together to account for emerging and novel pathogens, the geographic movement and global responsibilities of defense personnel, and the looming risk of catastrophic, possibly deliberate events. Stepping toward this, in 2020 the DoD shifted the lead responsibility for biosurveillance to the Office of the Under Secretary for Personnel and Readiness and set plans for a senior advisory group co-chaired with the USD(A&S).[83]

This may shift yet again, due to several factors. One is that DoD leadership is showing signs of becoming much more serious about addressing biological risks, including through execution of the first ever Biodefense Posture Review. While the 2020 directive holds many positive aspects, it was created in an environment of drastic cuts in biodefense. Another is the continuing pace of spread and evolution of SARS-CoV-2, which has clarified the need for an aggressive approach to pathogen early warning. The urgent threat that Russia may use weapons of mass destruction including biological weapons in the Ukraine war should play into the Department's early warning activities as well.

Two options would be moving forward with an integrated program under Personnel & Readiness, which would have the Defense Health Agency (DHA) serve as the hub of relevant activities, or to shift it to Acquisition and Sustainment. In either case, the high-level coordination set forth in the 2020 Directive will be necessary. The ultimate answer (between these or other options) should be informed by the best approach to creating an *early warning* system that helps address threats more effectively than at least some of the biosurveillance approaches in use today.

Pursuing the current plan would entail the Defense Health Agency (DHA) leading in biosurveillance and early warning—essentially, moving forward in executing the plan which has become somewhat stalled for the past two years. Responsible for the health care of civilian and military personnel,

83 DoD Directive 6420.02, DoD Biosurveillance, September 17, 2020.

DHA's TRICARE Health Plan has over 9.6 million global beneficiaries. In recent years DHA has been conducting a sweeping digital modernization effort called MHS GENESIS, which will be the common electronic health records systems across DoD and the U.S. Department of Veterans Affairs (allowing connectivity between when military personnel are on active duty to after they retire). As of June 2022, the system has been implemented at approximately 1,590 locations and is over halfway to its goal of completion by the end of 2023. Once complete, MHS GENESIS will provide one of the most globally diverse data sets, enabling syndromic surveillance through the Armed Forces Health Surveillance Branch's electronic surveillance system, akin to ESSENCE and National Syndromic Surveillance System discussed in the previous report.

Given these responsibilities, and those of GEIS, DHA should always have central roles in biosurveillance. Yet there are emerging questions of whether DHA serving as the leading agency best serves several important needs. For one, the task of general force healthcare is already vast, leading to concerns that improving and deploying more advanced technologies may not always be championed by DHA leaders who have vast responsibilities. The best node of DoD for tying to public health entities and global health security risks, and sharing data back, is another question. Still other considerations include the best structure to ensure close ties to WMD-focused intelligence and analysis, and how different entities work with nongovernmental innovators.

A shift in the lead DoD agency to A&S would likely involve a central role for the Defense-wide Chemical and Biological Defense Program (CBDP), within the Office of the Under Secretary for Acquisition and Sustainment. This could improve the connectivity of biosurveillance efforts across the Department given that CBDP is already the leader across DoD on research, development, and acquisition for countering chemical and biological threats and its reach includes force health protection. Other advantages could include ensuring that early warning efforts are informed by CBDP's cooperation with many international partners (including information sharing on how tech developments are advancing), which may also help form a pathway to reviving how international

biodefense partnership programs serve as vehicles for deploying new tools (see more on this in the international chapter next). Issues to accommodate would need to include ensuring that CBDP does not neglect biological threats compared with its chemical defense activities in the future, which can be addressed through leadership, internal oversight, and increased funding.

However DoD seeks to reorganize internally to best drive pathogen early warning toward more of a systems approach, several principles should provide guidance. Biosurveillance and early warning activities should be conducted and overseen in a manner that:

- Ensures science and technology advances are persistently leveraged in domestic and international settings
- Ties to deterring biological weapons threats, and what we learn about these potential threats from other countering weapons of mass destruction activities
- Creates feedback loops with data accumulated over time for continuing improvement and informing changes (as compared to being used largely for immediate responses)
- Can adequately scale up for potentially extreme events
- Conducts annual exercises and reviews to ensure defense biosurveillance efforts are increasingly synced and creating true early warning capabilities

Ultimately, pathogen early warning is central for reasons that include but extend well beyond force health protection. In the bigger picture, we recommend that the best organizational scheme for driving a systems approach to pathogen early warning should be informed by the increasing need for DoD to lead in deterrence against deliberate biological threats, the need to stay deeply attuned to the evolving biotech landscape globally, and the need to connect to global efforts toward early warning (addressed in the next chapter) and the aforementioned upgrades being made by the private sector and public health agencies alike.

EARLY WARNING FOR THE DEPARTMENT OF DEFENSE

The Department of Defense (DoD), as the largest U.S. government agency with over 2.9 million military and civilian personnel at approximately 4,800 locations in 160 countries, has a unique need for pathogen early warning.[84] One factor in this stems from DoD's mission to "provide the military forces needed to deter war and ensure our nation's security." To do this, DoD needs to be able to deploy forces and project power when and where needed. An example of this occurred in February 2022 during Russia's build-up of forces and eventual invasion of Ukraine when 8,500 service members from various sites in the United States, Germany, Italy, and Greece were deployed to eastern Europe as part of NATO's Very High Readiness Joint Task Force.[85]

Ensuring personnel are ready to deploy and execute missions means that the military chain of command needs to understand the risk posed by biological threats—whether it be from an adversary's use of a biological weapon, a leak from a biological laboratory, or a naturally occurring event. Pathogen outbreaks can also uniquely affect military forces as military personnel often work in close quarters and live in close proximity to each other for extended periods of time, especially on ships, in barracks, and in field conditions. Just as leaders need to be able to recognize tactical changes in the battlespace, these same leaders need an early warning system so they can understand what is an abnormal change from the typically encountered types of pathogens and their associated level of sickness. Beyond recognizing these changes, the armed forces also need to recognize if an adversary intentionally released a pathogen, so that attribution can be established and national leadership notified. With robust intelligence, surveillance, and reconnaissance systems, the DoD already conducts missile and force movement early warning well, as evidenced during Russia's buildup of forces on Ukraine's border and ranging back to the Cuban Missile Crisis. Now, each of the armed services needs to take a similar approach to biological threats and ensure their commanders are prepared, providing them with adequate pathogen early warning.

One near-term advancement should be to immediately leverage wastewater surveillance systems originally established to address COVID-19, which also played a crucial role in understanding the extent of polio outbreaks in New York this past summer. To expeditiously leverage this technology as an operational readiness initiative, services could fund wastewater surveillance pilot programs at select overseas installations and on deployed naval vessels as part of their pathogen

84 U.S. Department of Defense, "About," accessed November 3, 2022.

85 Scowcroft Center Task Force on Deterrence and Force, "Defending every inch of NATO territory: Force posture options for strengthening deterrence in Europe," *Atlantic Council,* March 9, 2022.

early warning approaches. Then, applying best practices, this work could be scaled-up to a DoD-wide program. Extrapolating from previous studies, price estimates may range from around $7,000 upward annually per sample site to leverage existing private sector capabilities, which could easily be done at numerous sites as a pilot program.[86] This would involve DoD personnel taking three small vial samples manually from a tank or pipeline or purchasing an automated sampler. Then, twice a week, the samples would be mailed to a laboratory in the U.S. for testing, with results being sent back securely and electronically within 36 hours of receipt. While this method would work for overseas bases and ships in a strike group with mail service, it would not be feasible for submarines or surface ships deployed independently. However, if the pilot succeeds, this restriction and the mail-induced lag time could be addressed by services training their own personnel to conduct the processing or embarking specialists to do so. Starting this as a pilot program would give services time to generate data in support of establishing wastewater surveillance as service-specific or a DoD-wide program of record in the next budget cycle.

86 Biobot Analytics, "Community COVID-19 Report," accessed November 8, 2022; Jillian Wright et al. "Comparison of high-frequency in-pipe SARS-CoV-2 wastewater-based surveillance to concurrent COVID-19 random clinical testing on a public U.S. university campus," *Science of the Total Environment* Vol. 820, No. 152877, 2022.

Implementation & Integration Across Biodefense, Public Health, and Technology Development

The sections above highlight two of the U.S. departments with leadership roles in creating the pathogen early warning capacities needed. How work is integrated across them will likely remain a multidimensional enterprise by which integration across health and defense agencies at multiple levels of government, and with nongovernmental and international partners, occurs across many axes.

To begin with, the United States must have a strong policy framework in place, routine and event-based cooperation across countless actors, strong collaboration between the public and private sectors, and connectivity with networks internationally. Luckily, many such elements have long been in play in the United States, as described earlier in this chapter, and more pieces have advanced well in recent years.

For example, the U.S. government is taking on board broader definitions of biodefense and biosecurity that account for the wide spectrum of biological risks in the world, and the overlap in how to pursue activities to understand and address them. This is important for efficiency and for preventing gaps. For example, the National Biodefense Strategy defines biodefense with appropriate breadth to serve early warning purposes by ensuring coverage of:

- Actions to counter biological threats, reduce biological risks, and prepare for, respond to, and recover from biological incidents;
- Pathogen threats that are deliberate in origin, accidental, or naturally occurring, and;

- Those that may impact human, animal, plant, or environmental health.[87]

This definition inherently shapes the perspective of what constitutes biodefense risk, and invites the collaborative participation of multiple agencies in order to address it.

U.S. policy should aim to build a resilient early warning system that is flexible and agile, and can target all emerging threats: including those not listed on the U.S. Select Agent List or Australia Group pathogens. As described earlier, the AP3 and other recent policy updates are set to accelerate this shift away from traditional threat agent lists, though individual departments and agencies will need to provide internal strategy and budgetary guidance to ensure the White House's policy directions are implemented effectively.

Importantly, DoD's policy framework has internally been shifting toward this definition as well. In a 2021 memo from Secretary of Defense Lloyd Austin, he instructed that DoD "will prioritize biodefense across the full spectrum of biological threats, from naturally occurring to accidental and deliberate biological incidents."[88] Prior to this, and mirroring the de-prioritization of addressing biological risks, DoD's approach to this mission grew more and more narrow as it cut budgets in this area, which contributed to a strong focus on specific known pathogens and operating in an environment in which adversadries had used biological weapons being the primary driver of many of the Department's efforts. This is not only an overly narrow view of how to meet national security needs, but also misreads how disease threats are evolving and whether other agencies can adequately meet defense early warning needs without DoD playing a strong and central role.

An early, forthcoming test of this will be DoD's first-ever Biodefense Posture Review (BPR), which is likely to be released in early 2023. It should elevate, strengthen, and properly resource Department-wide efforts to deter, detect,

87 The White House, "National Biodefense Strategy and Implementation Plan," October 18, 2022.

88 Secretary of Defense, "Biodefense Vision Memo," November 1, 2021.

and respond to natural, accidental, and deliberate biological events. This integrated approach will be central to DoD's design and deployment of early warning systems to counter future outbreaks and deter the adversary development and use of biological weapons against the United States, its allies, and partners. The BPR also presents the opportunity to evaluate the performance of the biosurveillance program under the structure set forth in the 2020 directive described above, and potentially realign roles and responsibilities if that is warranted for the pursuit of enhanced pathogen early warning.

As DoD and other departments and agencies further extend national policy shifts in their internal instructions, stakeholders in Congress and the public should expect this to manifest in significantly increased resourcing, beginning with the President's Fiscal Year 2024 Budget Request. Guidance from the Office of Management and Budget should direct large funding increases to the DoD biodefense programs. Further, the direction provided in an October 2022 National Security Memorandum to begin assessing and tracking biodefense budget trends should kick off annual evaluations of progress, which should be informed by gap analyses and technology reviews to ensure strong tools are integrated to improve early warning as soon as possible.[89]

Moreover, in order for this pattern of policy instruction informing investment decisions to drive real progress, it must be supported by human collaboration, in particular across key U.S. federal agencies.

Interagency Integration

Creating effective early warning with input from all relevant U.S. federal agencies will be even more complex than just integration across HHS and DoD (with the Office of the Director of National Intelligence's Counterproliferation and Biosecurity Center serving as the integration lead for the U.S. intelligence community for foreign biological threats, including potential pandemic disease outbreaks). Ongoing and future programs by

89 The White House, "National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security," October 18, 2022.

the National Labs, Department of Homeland Security, U.S. Agency for International Development, and others need to be woven together effectively with an aim toward better early warning.

Department of Homeland Security

Within the United States, contributions to early warning by the Department of Homeland Security (DHS) include research and development, and the operation of several surveillance and early warning programs that include detection systems, information platforms, and several unique early warning tools. Many of these are focused on terrorism risks, and most benefit from bringing information together for rapid sharing across local, state, and federal actors. Some DHS programs currently aim to enhance detection and early warning of a biological event at a specific location, for example major cities, transportation nodes, or sites that host large crowds for events.

DHS was a relatively early mover toward more actionable biosurveillance within the United States. This began with its launch of the BioWatch Program in 2003, which now operates in around 30 U.S. cities. While it represented a major step forward in the pursuit of timely, actionable early warning of a biological event, the BioWatch Program has faced implementation challenges.[90] Forward-looking programs by DHS include Biological Detection for the 21st Century (BD21), which aims for a system-of-systems approach to incorporate more advanced tools and better integrate information, and a crowd-sourcing effort called the Enhanced Passive Surveillance Program that aims to collect information from veterinarians and others that would provide early warning of a emerging disease outbreaks in livestock, among others. However, BD21 has faced several programmatic pauses as concerns over the technology's acquisition put the program at risk of losing funding.[91] It is particularly important that U.S. government leaders move forward quickly to shape future plans for BD21 and other DHS

---

90 Ben Fox, "Audit finds major gaps in US bio weapons detection system," *AP News*, March 4, 2021.

91 Carrie Cordero, Asha M. George, "Opportunity to Reform the Department of Homeland Security's Biodefense Operations and Governance," Lawfare, May 24, 2022.

initiatives, and resolve how they will integrate with the CDC's Center for Forecasting and Analytics, DoD's early warning entities, and others.[92]

The National Labs

The Department of Energy (DOE) operates 17 National Labs across the United States that provide the expertise and agility required to tackle critical scientific challenges, including many functions that contribute to biosurveillance and early warning advancement. They possess unique instruments and facilities, many of which are found nowhere else in the world. They also hold great promise in public-private collaboration, and host multidisciplinary systems and approaches that are necessary for transitioning basic science into further early warning technological developments.

During the pandemic, the National Laboratory network assembled to create the National Virtual Biotechnology Laboratory (NVBL), which is a consortium aimed at integrating core strengths and capabilities relevant to the threats posed by COVID-19.[93] In order to improve COVID-19 responses, this consortium tapped into the power of DOE user facilities, which house advanced capabilities that scientists can use based on a competitive selection process. Such capabilities include light and neutron sources, nanoscale science centers, sequencing and bio-characterization facilities, and high performance computer facilities.[94] This integrated effort resulted in the evolution of effective testing capabilities, identification of new targets for medical therapeutics, enhanced epidemiological and logistical support, and harnessing manufacturing capabilities across the complex to address supply chain issues. It is noteworthy that the user facilities are available to academics and industry, providing a core repository of expensive state of the art resources and associated expertise to respond to emerging threats.

92 U.S. Government Accountability Office, Report to Congressional Requesters: Biodefense - DHS Exploring New Methods to Replace BioWatch and Could Benefit from Additional Guidance, 2021; William Beaver et al. *A Handbook for Ending Catastrophic Biological Risks*, Council on Strategic Risks, December 2021.

93 U.S. Department of Energy, "National Virtual Biotechnology Laboratory (NVBL)," accessed November 8, 2022.

94 U.S. Department of Energy, "Office of Science User Facilities," accessed November 11, 2022.

Subsequent to this initial and timely integration, the Department's Office of Science is also establishing a Bio-preparedness Research Virtual Environment (BRaVE) initiative to help ensure the development of scientific capabilities that aid in the prevention of and response to potential biological threats. This offers a unique and much-needed opportunity to tap into the state of the art resources that reside within the DOE's National Laboratory Network and pivot them to address biological threat challenges. Overall, the National Labs should be proactively included in a national early warning framework, including to ensure it continues to foster basic research being leveraged in continuing private sector innovation for early warning.

U.S. Department of Agriculture

The U.S. Department of Agriculture (USDA) will play an important role in pathogen early warning, given its oversight on crops and livestock populations. Biological threats do not solely consist of those that affect humans—deliberate or natural biological threats can kill massive amounts of livestock and crops, threatening food security and economic stability. Additionally, disease spillover from livestock populations into humans can initiate severe pandemics, as we have observed in swine flu outbreaks.[95] To contend with each of these threats, it is essential that USDA maintains strong biosurveillance networks on livestock and crops.

The 2022 National Biodefense Strategy recognizes the role that USDA will play in early detection, specifically mentioning USDA as a lead in a variety of early detection, sequencing, and reporting objectives.[96] Within USDA, the Animal and Plant Health Inspection Service (USDA-APHIS) is the natural lead on biosurveillance and early warning. APHIS has responsibility for a range of biological threat response activities, including in invasive pests, animal and plant imports and exports, and research on agriculturally relevant biotechnologies. Additionally, APHIS is the agency lead for the Select Agent Program, which regulates research and distribution of a list of biological agents and toxins with potential to pose a threat to human and animal

95 Harriet Constable, "The Reasons Swine Flu Could Return," BBC, February 1, 2021.

96 The White House, "National Biodefense Strategy and Implementation Plan," October 18, 2022.

safety.[97] In February 2022, APHIS laid out a strategic framework to develop an early warning system for emerging and known zoonotic threats, including SARS-CoV-2.[98] This plan will make use of $300 million in funding from the American Rescue Plan. This investment will be essential in fortifying biosurveillance and increasing awareness of potential emerging threats, and should be expanded as APHIS scales up its early warning work.

U.S. Fish and Wildlife Service

The U.S. Fish and Wildlife Service (FWS) is responsible for managing and maintaining wildlife and wild habitats in the United States. This role positions FWS as an important domestic player in reducing biological threats, through maintaining pristine environments, regulating the import of wildlife that may carry infectious diseases, and monitoring disease in wildlife populations.

Funding from the American Rescue Plan will augment FSW's capacities in each of these areas.[99] Perhaps most importantly, it provides $45 million to FSW to strengthen early detection, management, and response to contain disease outbreaks in wildlife populations. This funding will also go toward monitoring diseases that have the potential to cross species barriers, and will provide the initial investment needed to develop a national wildlife disease database. Using this funding, FSW has established the Zoonotic Disease Initiative, a three-year grant program providing funding to Tribes, states and territories to improve detection and early warning for pathogens with the potential to cross over into human populations. In September 2022, FSW announced $6.3 million in grants to Tribes and states working related projects, many of which take a One Health perspective, meaning that they approach human health, animal health, and environmental health as an interconnected whole.[100]

97 Federal Select Agent Program, "Select Agents and Toxins," 2022.

98 U.S. Department of Agriculture, "APHIS Announces Final Strategic Framework for Enhancing Surveillance for SARS-CoV-2 and other Emerging Diseases Under the American Rescue Plan," February 9, 2022.

99 U.S. Fish and Wildlife Service, "American Rescue Plan Provides Critical Support for U.S. Fish and Wildlife Service Programs," March 12, 2021.

100 U.S. Fish and Wildlife Service, "$6.3M Awards Fund Wildlife Disease Prevention and Preparedness," September 20, 2022.

The American Rescue Plan also allocated $10 million to support implementation of the Lacey Act, which restricts importation of animals that may bring negative effects to humans and animals in the United States. In recent years, the Lacey Act has been applied to restrict the importation of salamanders that may carry the pathogenic chytrid fungus,[101] and it may be a valuable tool in restricting wildlife imports that potentially carry pathogens that could impact humans. Additionally, FWS implements the Law Enforcement Management Information System (LEMIS), which contains basic data on imports and exports of wildlife products and live organisms. Given the demonstrated disease risk posed by wildlife trade, data in the LEMIS database is a valuable data input for pathogen early warning.[102] However, LEMIS data is not permanently archived nor shared publicly, so increased transparency would make the database a more valuable resource for early warning.[103]

Finally, the American Rescue Plan provides $20 million in funding to advance wildlife inspections. While there is little public information about progress on this front, hiring more skilled inspectors at ports is an important step in ensuring that biological threats do not enter U.S. borders, and that any anomalies or concerns are quickly reported and addressed.

The United States Geological Survey

The U.S. Geological Survey (USGS) conducts biosurveillance and mapping research that is useful for risk forecasting, situational awareness, and early pathogen detection. Through mapping the distribution of disease in animal populations, USGS provides useful situational awareness and the ability to note anomalies and changes in disease dynamics. In 2015, USGS surveillance of avian influenza in wild birds enabled the agency to alert USDA about the

101 Michael J. Bean, "Injurious Wildlife Species; Listing Salamanders Due to Risk of Salamander Chytrid Fungus," *The Federal Register,* January 13, 2016.

102 The Nature Conservancy, "Wildlife Trade a Key Risk Factor in the Global Spread of Infectious Disease," July 7, 2021.

103 Evan A. Eskew, "United States wildlife and wildlife product imports from 2000–2014," *Sci Data* Vol. 7, No. 22, 2020.

increasing threat to the poultry industry.[104] Additionally, USGS manages the Wildlife Health and Information Sharing Partnership-event reporting system (WHISPers), a web-based repository for sharing basic information about wildlife death and illness events, including disease on-set dates, species affected, and locations.[105] This data is provided by natural resource managers and other environmental stakeholders. Though WHISPers is not comprehensive, it seeks to provide natural resource managers with timely information on wildlife disease to enable better preparedness.

Funding from the 2020 Coronavirus Aid, Relief and Economic Security (CARES) Act has enabled USGS to expand its biosurveillance and early warning capacities. Some of this funding has supported the North American Bat Monitoring Program, which coordinates regional data collection efforts to map where North American bats live and how their populations interact with humans.[106] Part of this project involves assessing the risk of North American bats becoming infected with COVID-19. Additionally, CARES Act funding has gone to standing up the Disease Decision Analysis and Research (DDAR) team, which works to provide actionable information to decision-makers regarding zoonotic disease risk and mitigation measures.[107] To aid in understanding COVID-19 prevalence, USGS has supported the National Wastewater Surveillance System in detecting SARS-CoV-2 through high-frequency wastewater sampling, enabling a higher resolution picture of disease trends.[108]

104 National Wildlife Health Center, "Avian Influenza Surveillance," *U.S. Geological Survey*, October 16, 2022.

105 National Wildlife Health Center , "WHISPers," *U.S. Geological Survey*, July 1, 2019.

106 Ecosystems, "Tracking Bats and Coronaviruses," *U.S. Geological Survey*, September 19, 2022.

107 Ecosystems, "COVID-19 Pathways and Wildlife Dynamics," U.S. Geological Survey, September 19, 2022.

108 Meghan M. Holst et al. "Rapid Implementation of High-Frequency Wastewater Surveillance of SARS-CoV-2," *ACS EST Water* Vol. 2, No. 11, 2022.

USAID boosts disease surveillance across borders in Southeast Asia.
Richard Nyberg, USAID

U.S. Agency for International Development

The U.S. Agency for International Development (USAID) has implemented a variety of initiatives to support global health and prevent the spread of infectious diseases. Over the past ten years, USAID's Global Health Security program has invested over a billion dollars in strengthening partner countries' abilities to detect and respond to endemic and emerging diseases.[109] USAID funds projects focused on building human capacity in disease surveillance, building surveillance and diagnostic systems, and improving detection and reporting of zoonotic diseases.[110]

One of USAID's most relevant projects to early warning is the Strategies to Prevent Spillover (STOP Spillover) program, which began in October 2020.[111] STOP Spillover works in select Asian and African countries to support efforts in monitoring priority pathogens and implementing risk reduction measures. So far, this program has mainly worked to identify gaps in knowledge, identify key stakeholders, and determine the most significant threats and best intervention measures for each region of interest. USAID has supported the establishment of technical working groups to design and implement intervention

109 U.S. Agency for International Development, "Global Health Security."

110 U. S. Agency for International Development, "Partnerships for a More Secure World."

111 Tufts University Consortium, "STOP Spillover Year 2 Semi-Annual Report," April 2022.

measures. A few examples of projects being taken on by these working groups include engaging with communities to encourage limited contact with animals, providing better protection of drinking water from bat excrement, characterizing bat populations and bat-human interactions, and working to improve biosafety on farms. These efforts and others aim to reduce the risk of disease spillover, and also help develop early detection infrastructure.

STOP Spillover is a successor to a USAID program called PREDICT, which was canceled in March 2020. Some of PREDICT's partnerships generated controversy, as partner organizations conducted research involving the manipulation of viruses[112] and the active collection and analysis of animal samples in the wild.[113] Both of these processes involve biosecurity and biosafety risks, and have the potential to be extremely dangerous if any human error occurs. Under PREDICT, scientists collected 140,000 biological samples and discovered 1,000 new viruses, but it is yet to be seen if this work will have utility in preventing future pandemics. While USAID indisputably plays an essential role in disease readiness, detection, and early warning, partnerships and research tactics must be thoughtfully considered. STOP Spillover appears to be moving in a safe, secure, and productive direction, and it is important that this trajectory continues and that potentially dangerous research is kept to a minimum.

Across all of these agencies, a central, overarching question continues to linger: How will the U.S. government bring these important efforts together? This is important for the sake of efficiency and prioritization, but also for leveraging these early warning capabilities into a systemic approach that is even more impactful than the sum of its parts.

Much will come down to two factors: how the CDC decides to approach the CFA's role for the U.S. interagency, and how DoD chooses to reorganize its biosurveillance and early warning efforts. Relevant leaders in the U.S. government should set the strategic direction on these two factors as soon as possible.

112 Amber Dance, "The shifting sands of 'gain-of-function' research," *Nature News,* October 27, 2021.

113 Donald G. McNeil Jr. and Thomas Kaplan, "U.S. Will Revive Global Virus-Hunting Effort Ended Last Year," *New York Times,* August 30, 2020.

Such direction can then begin to shape practical and programmatic details that will be key to implementation. One significant issue is whether the CDC's data sharing arrangements, which are coordinated with individual states, will limit its own forecasting abilities and its ability to collaborate with other federal agencies such as DoD. This was historically a challenge between the two agencies. It is more pressing with the drive toward early warning; data shared from U.S. states and localities hitting the federal government over weeks or months may simply be less useful for early warning purposes, even if it can still be helpful in longer-term research and forecasting.

Other implementation questions will include whether and how to co-locate personnel and assets across federal agencies, for example DHS's BD21 and DoD personnel with the CFA. Personnel, physical asset, and data sharing are all likely to require legislative authority adjustments, agreements between federal agencies, or both. Still another set of implementation questions pertain to whether the shifting early warning landscape warrants changes to interfaces with emergency response entities within the United States. For example, given the constitutional and practical questions pertaining to defense force activities within the United States, state and federal leaders, the National Guard, NORTHCOM, and others should ensure they are positioned ideally in case improved early warning triggers different patterns of responses in the future.

Though complicated, these elements of U.S.-focused integration are solvable. Moreover, they must be addressed in the near term given that further collaboration with international actors is proceeding to expand—and should continue to do so.

A comprehensive and robust early warning system is likely to require collaboration across agencies and cross-functional partners. A historical lens has taught us that a frequent review of tools, like early warning systems, is necessary to ensure not only efficacy but also operational effectiveness. It is recommended that early warning systems undergo routine assessments for quality assurance and output. These stress tests can and should include exercises, cross functional partner evaluations, and even external review. Such

efforts provide an opportunity to assess if the existing framework and systems are still addressing the foundational needs of specific agencies, communities, and regions.

The new annual U.S. exercise program directed by National Security Memorandum 15 described above will contribute strongly. Ultimately, the goal is to not only exercise the functionality of the early warning program, but also the response that is initiated by signal events. Exercises, quality metrics, and stress tests of early warning programs will help ensure oversight, but also opportunities for improvement.

They will also be instructive to an even bigger need: ensuring robust international cooperation.

International Collaboration

Emerging biological threats can be first evidenced within or outside of the United States. Moreover, significant early warning capacity exists around the world and this is expanding. Whether and how it will come together, and how the United States sets itself up to best interface with these capacities, remain open questions (discussed further in the next chapter).

Several public health surveillance systems globally seek to help integrate early warning and surveillance data generated. Examples include the Global Influenza Surveillance and Response System run by the World Health Organization, and the Joint FAO–OIE–WHO Global Early Warning System for health threats and emerging risks at the human–animal–ecosystems interface.[114] It is imperative that individual governments track and shape how these and other systems are evolving to build resilient and collaborative interfaces based on learning during the COVID-19 pandemic. For instance, at the seventy-fifth World Health Assembly in May 2022, the Director General of WHO set out ten proposals to strengthen the global architecture for health

114 GLEWS, "About GLEWS and GLEWS+," accessed November 8, 2022.

emergency preparedness, response, and resilience.[115] This report was generated with participation from over 300 global entities, and involves a synergistic assimilation of global strengths and weaknesses.

How exactly international changes and capacities integrate with U.S. systems remains another open question that should be addressed. This should begin with what is already occurring. The CFA is reportedly expanding its international data sharing and collaboration, with plans to continue this buildout. At the same time, DoD already brings in many international inputs through its Global Emerging Infections Surveillance (GEIS) program. Even just considering these two major streams, the question remains: will these entities focus on unique international and domestic inputs and then fuse these together (alongside other agencies and inputs)? This question warrants near-term consideration and decision-making, which should proceed from both the Executive Branch and Congress. Considerations in creating this map toward international integration should include the best arrangements to progress toward pathogen-agnostic work, ensuring that data sharing issues will be overcome, and how DoD itself chooses to organize internally.

Public-Private Collaboration

The COVID-19 pandemic has resulted in the most rapid global development and deployments of testing and surveillance programs in modern history. The speed at which COVID-19 tests were developed and operationalized across the world was not only unprecedented, but also resulted in developments of early warning systems that extended beyond diagnostic needs and existing partnerships. Continuing, significant progress in pathogen early warning will require greater public-private collaboration, from early-stage research to technology deployment and operations.

The private sector, especially since COVID-19, has shown strong capabilities in establishing surveillance and early warning systems, whether those be

115 WHO Draft for Consultation, "10 proposals to build a safer world together: Strengthening the Global Architecture for Health Emergency Preparedness, Response and Resilience," June 2022.

testing or syndromic surveillance.[116] As a result, there is ample opportunity for information sharing and data collection, but also future partnerships and collaborations that may build even more resilient early warning systems.

COVID-19 has changed the dynamics of early warning and infectious disease testing capabilities and capacity. Once available to healthcare providers and public health agencies, SARS-CoV-2 tests became widely available and testing companies were soon in high supply, allowing companies and many in the private sector to have access to diagnostic tools. As a result, many industries opted to implement early warning systems to act as a COVID-19 surveillance strategy that would not only help reduce transmission within the workplace, but also serve to support employees returning to work during a pandemic. For many industries to return to work, such as professional sports and entertainment, surveillance systems were put in place to ensure routine testing.[117]

Such efforts required considerable financial investment and coordination with laboratories, but may not have translated to information sharing or collaboration with cross-functional partners. Continuing public-private collaboration is important for expanding this work into real information sharing, which avoids information asymmetry and ensures the end user is provided with the accurate and timely information necessary to make informed decisions . It is also important to determine scope for future early warning activities. For example, several industries did routine SARS-CoV-2 testing for their employees, but struggled to determine the best testing platforms or cadence of testing.

Additionally, academic research, as funded by agencies such as the National Institutes of Health, has built multinational partnerships and global health frameworks for decades. These frameworks, being built for research purposes, have a certain agility incorporated into them, while ensuring compatibility with

116 Andrew Guard et al." Facilitating national football teams return to training and competition during the COVID-19 pandemic," *BMJ Open Sport & Exercise Medicine* Vol. 8, 2022.

117 Christina Mack et al. "414 Population testing for COVID-19: an approach for infection prevention," *British Journal of Sports Medicine* Vol. 55, 2021; James Dove et al. "COVID-19 and review of current recommendations for return to athletic play." Rhode Island medical journal Vol. 103, No. 7, 2020; Monona Rossol, "Comparison of Two Entertainment Industry COVID-19 Programs," *NEW SOLUTIONS: A Journal of Environmental and Occupational Health Policy* Vol. 32, No. 3, 2022.

safety and efficiency. Harnessing insights from such frameworks—and the decades of knowledge on the advantages and challenges associated therein—can greatly strengthen our ability to counter emerging threats. They can also facilitate the design of robust yet flexible systems, which can be tuned to incorporate new findings and processes. Indeed, countering and warning regarding an emerging unknown threat is always, in some regard, a research exercise.

One of the keys to progress for achieving true pathogen early warning will be for the federal enterprise to engage in active and dynamic partnerships with the bio-industrial base. This will take various forms moving forward, yet it is clear that some of the biggest gains have been made by public-private partnerships. Both Operation Warp Speed and the RADx Initiative delivered key medical countermeasures and diagnostic tests through concerted collaboration utilizing different models for development, testing, and acquisition.

Setting productive models for public-private collaboration is growing even more important given multiple breakthroughs in private sector progress that could greatly enhance early warning. Many stem from the growing use of AI/ML tools.[118] Another example has been the development by Ginkgo Bioworks and Draper Laboratories under the Finding Engineering-Linked Indicators (FELIX) program administered through the Intelligence Advanced Research Projects Activity.[119] Ginkgo Bioworks developed a computational platform, the Engineered Nucleotide Detection and Ranking (ENDAR), to analyze next-generation sequencing data of complex biological samples at scale.[120] ENDAR is designed to be implemented across the early warning landscape, providing information about the samples with genetically engineered regions, the origins of the novel and/or spliced genes, and if the signatures within the engineered organism provide details on specific intent for the organism's

118 Pattern Computer, "Pattern Computer ProSpectral COVID Detector Finds 100% of Positives" December 8, 2021.

119 *IARPA, Ginkgo Bioworks and Draper Announce New Technologies to Detect Engineered DNA*. *YouTube*. October 17, 2022.

120 Riley Griffin, "Ginkgo Is Trying to Detect Future Man-Made Biological Threats," *Bloomberg*, October 17, 2022.

use.[121] Also under project FELIX, Draper Laboratory developed new tools for the detection and computational analysis of genetically engineered pathogens, centered on their Targeted Engineering Marker Sequencing detection method, or TEM-Seq. Draper engineers developed a new microarray design and computational analysis package that enable an environmental or biological sample of as little as 10 µL for TEM-Seq detection.[122] The results of Draper's work are an important step for massively multiplexed detection of genetically engineered material, especially for fieldable detection of low concentration targets within complex environmental samples.

Draper, which is a nonprofit laboratory, is working on several additional projects that will advance early warning capabilities. One is the DIGET (Detect It with Gene Editing Technologies) program, in which Draper incorporated MRIGlobal's CRISPR-based assay into fieldable and rugged detection device capable of running a sample against 1,000 biomarkers for detection of known, novel, or engineered organisms within 15 minutes at less than $10 per run.[123] The advantage of this system is that the biomarkers selected for the CRISPR-based microarray are expected to be reconfigured within a 24 hour window, a considerable advantage for detecting novel and engineered pathogens in a deployed setting.[124]

Another extremely promising example is the Nucleic Acid Observatory (NAO), a group spun out of MIT Media Labs and is developing a platform for early pathogen detection in a pathogen-agnostic manner, by metagenomic sequencing of the environment. NAO aims to perform environmental surveillance and analysis of international airports or wastewater, given that it has established infrastructure and protocols for sampling. Furthermore, mechanisms like wastewater surveillance provide personal anonymity, thus

121 Ginkgo Bioworks and Concentric by Gingko, "An Early Warning System for Engineered Biological Threats," October 2022.

122 *IARPA, Ginkgo Bioworks and Draper Announce New Technologies to Detect Engineered DNA*. *YouTube*. October 17, 2022.

123 Author background interview with subject matter expert following Chatham House Rules, September 19, 2022.

124 Draper, "Draper to Develop Biosurveillance Technology for DARPA to Counter the Rapid Spread of Pathogens," May 6, 2021.

circumventing some potential data privacy issues. In particular, NAO will emphasize detection of pathogens engineered to spread exponentially over prolonged asymptomatic infection, similar to the mechanisms and spread of HIV. Their platform will perform metagenomic sequencing on environmental samples, amplify and analyze sequences for known pathogens, and detect exponentially growing novel sequence fragments that are dissimilar to known pathogens and potentially engineered.[125] Novel sequences can be examined to determine whether the genome is engineered, which may subsequently trigger established mechanisms to rapidly stop transmission of a novel pathogen as well as develop diagnostics and therapeutics.

Some of these advances may be carried forward by relatively traditional models: the U.S. government acquiring tools or paying for their creators to operate them with predefined scope and time periods. Yet these examples show how quickly the early warning toolset is expanding. Ensuring that public-private collaborative models continue to foster such progress and prevent lock-in with technologies that may quickly be overtaken by more advanced ones will become even more pressing in the years ahead.

Conclusion

The early warning progress made within the United States in recent years has been substantial. As this chapter described, several big questions must be resolved in the near-term to ensure this foundation persists and that the United States continues to build upon it in the decades ahead. The potential gains in pandemic prevention, general health security, and deterrence are significant. Of course, how the United States proceeds to iron out these issues and continue progressing must tie to how pathogen early warning is advancing around the world, which is the focus of the next chapter.

125 The Nucleic Acid Observatory Consortium. "A Global Nucleic Acid Observatory for Biodefense and Planetary Health," *arXiv*, August 2021

Satellite view of the Black Sea, Mediterranean Sea, and Caspian Sea.

Norman Kuring / NASA

IV. Advancing Global Early Warning

U.S. efforts to build an effective domestic pathogen early warning system across the Centers for Disease Control and Prevention, Department of Defense, other federal agencies, and numerous other actors are good starting points. The resources, reach, and expertise that Washington and the U.S. private sector can bring to bear are critically necessary for any comprehensive early-warning network.

But biological risks and infectious diseases do not respect national boundaries. As the COVID-19 pandemic clearly demonstrated, novel pathogens can spread easily without adequate systems in place—quickly outstripping national capacity and rendering purely domestic responses largely ineffective. A threat anywhere is a threat everywhere, especially when it comes to diseases that lack well-established and easily-accessible medical countermeasures. An effective early warning network must, therefore, have some level of global coverage to be effective.

As COVID-19 also demonstrated, however, not all states have the same, or even similar, foundational responses to infectious disease threats. Pathogens may know no borders, especially due to the impacts of climate change,[126] but a country's capacity to prevent, identify, and respond can differ radically, with serious implications for global response. Some states may have the political will, but few resources; others may have resources, but little political will. Some may have neither. A comprehensive and effective early-warning network must take these differences into account—acknowledging, addressing, and supplementing gaps in capacity across different states and regions. Moreover, an effective early-warning system requires continued investment and agility to ensure efficacy: it should not be a box to check, but rather an iterative and evolving tool designed to address ever-changing threats.

126 Camilo Mora, et al., "Over half of known human pathogenic diseases can be aggravated by climate change," *Nature Climate Change* Vol. 12, 2022.

In the past and currently, U.S. collaboration with partners around the world that relates to early warning has taken many forms. Many partnerships are fostered by the CDC, HHS, National Labs, and other agencies, spanning from scientific collaborations to epidemiology training to collaborative clinical work that contributes to how the global community identifies and understands disease threats.

Biodefense, biosecurity, and military medical cooperation have always formed unique and crucial lines of effort as well. For the United States and many of its partners around the world, biosurveillance and early warning capacities focus on protecting the unique health needs of defense forces, diplomats, and other personnel, and they are directed at deterring a few countries from the use of biological weapons and reducing the impact if such an attack is carried out. This ranges from remote locations in Africa that housed special operations forces where personnel could have been exposed to unique disease threats, to densely urban areas of Northeast Asia that may be targeted with biological weapons.

Importantly, all of this cross-sectoral work also drives toward transparency and trust, safety and security (including around labs that contain highly harmful pathogens), the implementation of nonproliferation treaties, and the upholding of norms regarding peaceful applications of advances in the life sciences.

Many experts have posited the need for a global pathogen early warning system for which the main components are regional hubs that serve the unique needs of different populations while adopting common, collaborative approaches that allow for data and analysis to be rapidly shared internationally. In CSR's 2021 report, we recommended that the build-out of such early warning capacities should "hook into enduring missions, targeting some investments to leverage activities that tie to enduring national needs, such as biodefense efforts, and that expanding cooperative biological engagement programs for building out early warning system components should be prioritized."[127]

127 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, July 2021.

Just as the scientific, public health, and biodefense sectors must unite in pursuit of early warning within the United States, creating global early warning progress is requiring continued work across such sectors as well. This chapter outlines examples of this dynamic around the world, focused on national and regional efforts that should be leveraged as foundations for regional early warning hubs or centers of excellence.

The chapter begins by describing the background and current status of several candidate countries and entities, then describes a few examples of international progress that may help tie such efforts together at a global scale, and help achieve broad international security objectives.

Regional Early Warning Hubs: Building on Health Security and Biodefense Capacities

Several regions around the world and many individual states have seen incredible progress in health security and biodefense in recent decades, including in biosurveillance and the deployment of tools and knowledge needed for early warning. The background of such efforts shows deep work in tailoring progress to the needs and disease threats of different populations. It also showcases that in many parts of the world, cooperation among defense, health, and scientific agencies is already routinely operationalized in ways that can be leveraged in further advancing early warning capabilities. This section will highlight some of these examples, beginning with Central Asia and the Caucasus, followed by Africa, Southeast Asia, the Middle East, and Australia and New Zealand. This list is not exhaustive; instead, it represents several examples of clear progress toward pathogen early warning that other states or organizations could leverage in the coming years.

Central Asia and the Caucasus

For multiple historical reasons, the region of Central Asia and the Caucuses should be viewed as a high priority for expanding biosurveillance and early warning hubs in the coming years. The region already holds a history of biosurveillance cooperation across nations, as well as a strong foundation of technology and human expertise. Cooperation among nations in the region with the United States and the European Union, as well as with Russia and China, makes this a uniquely promising region as well.

Moreover, an important factor in making this cooperation a reality is that many of its nations already integrate well across public health and security agencies. This is partially a historical legacy: the collapse of the Soviet Union and subsequent events revealed that the nation had developed an industrial-scale biological weapons complex in the region. Many countries surged to assist in dismantling legacy biological weapons capabilities in Central Asia and to facilitate the direction of expertise toward peaceful pursuits. This work occurred alongside multilateral development assistance and public health collaboration aimed at bolstering stability in the region during this dramatic period of change. Many of the relationships fostered during this period have remained strong, and it has enabled a robust capacity for disease surveillance and early warning of emerging disease risks across the Caucasus and Central Asia.

This section describes capabilities in Georgia and Kazakhstan as examples, noting that other nations in this neighborhood have strong early warning foundations as well, and highlights the possibility of the Biosurveillance Network of the Silk Road becoming a key part of regional pathogen early warning.

Georgia

The Republic of Georgia was one of the earliest nations to develop diagnostic tests for COVID-19,[128] underscoring its strong capabilities in disease detection, characterization, and responses. This has been built over several decades of deliberate investments and collaboration with other nations that have been designed to account for the full range of biological threats. It is also a geographically unique nation in terms of future global early warning systems, given its proximity to Asia, Russia, the Middle East, and Eastern Europe.

HISTORICAL EFFORTS

In the early 1990s, Georgia's long history of focusing on endemic diseases and especially dangerous pathogens was set back by the dissolution of the Soviet Union and subsequent financial challenges. National leaders worked internally and with international partners to come out of this challenging period with a stronger health sector than ever, including with the establishment of the National Center for Disease Control (NCDC) in 1996.

In helping to establish the NCDC and other elements of Georgia's improved public health system, the U.S. CDC and USAID began support and collaboration with Georgia in the early 1990s, followed later by scientific cooperation with the U.S. Department of Health and Human Services. This augmented Georgia's support from the WHO, Doctors Without Borders, the government of Canada, and other partners.

Importantly, early disease detection has always been a primary objective for Georgia in the post-Soviet era. Indeed, the first joint conference between Georgia's NCDC and the U.S. CDC, held in 1996, focused on biosurveillance and information systems.[129] Going back to this time, Georgia was an early

128 U.S. Embassy in Georgia, "CTR-trained scientists develop diagnostic testing capability for COVID-19," April 23, 2020.

129 Republic of Georgia, National Center for Disease Control and Public Health, "20 Years," 2016, p. 10.

adopter of sequencing-based approaches and other advanced tools to improve its disease detection capabilities.

As part of its efforts to address WMD risks in the former Soviet Union, the U.S. Department of Defense began cooperation with Georgia in 1997.[130] This was expanded in 2002 with an agreement under the U.S. Cooperative Threat Reduction Program's bio arm, then called the Cooperative Biological Engagement Program (CBEP, later BTRP), to ramp up focus specifically on addressing biological threats, including those that could stem from deliberate sources: terrorists or other nations.[131]

The Georgia-U.S. partnership since that time has included numerous types of activities aimed at creating a holistic approach to biological risk reduction. As with many countries, these efforts included the consolidation of dangerous pathogen samples (used for public health and peaceful research purposes) into single, well-secured facilities with properly trained personnel. Biosafety and biosecurity improvements have also been major focus areas. Biosurveillance and driving toward early warning and understanding of biological threats have always remained central.

To make this work effective, and because Georgia has long adopted a One Health approach, the effort stems across the NCDC, agricultural and labor authorities, defense entities, and others. As such, it has long been a stand-out example of interagency, One Health-oriented collaboration serving health security and biodefense needs simultaneously.

Georgia also hosts strong physical infrastructure for this work. Its network of 22 laboratories operate under a unified national system in conjunction with the Richard Lugar Center for Public Health Research. As Georgia's primary lab and the region's only BSL-3,[132] the Lugar center plays a central

130 U.S. Department of State, "Agreement Between the United States and Georgia," November 10, 2022.

131 Congressional Research Service, "The Evolution of Cooperative Threat Reduction," November 23, 2015.

132 Caroline Schuerger, Sara Abdulla, Anna Puglisi, "Mapping Biosafety Level-3 Laboratories by Publications," *Center for Security and Emerging Technology,* August 2022.

role in disease surveillance across the country—monitoring smaller research facilities and providing quality control for testing efforts. It also serves as an example of the need for all nations to reduce risks by limiting access to dangerous pathogens and increasing lab security. CBEP supported the Lugar Center's construction,[133] and to this day, biosurveillance remains one of the lab's primary activities.

TECHNICAL CAPACITIES

Through the types of partnership described above and its national investments, Georgia's lab network and early warning capabilities operate on a strong technical backbone. In the early 2000s, the U.S. Department of Defense used the BTRP to advance capabilities for syndromic surveillance across partner nations such as Georgia. This included introducing the Electronic Integrated Disease Surveillance System (EIDSS) into Georgia and several other countries to serve as a central data system. Its software integrates clinical data into a single system for the partner nation to analyze both human and veterinary clinical case reporting.

The NCDC has also advanced its pathogen detection and diagnostic capabilities across its lab network - an effort that recently included a push toward more pathogen-agnostic tools. Georgia's labs integrated the use of a range of tools from the earliest days of the COVID-19 pandemic within the nation. Its work included PCR testing of wastewater in May-June 2020, real-time PCR testing in suspected patients, serum sampling and analyses, and using next-generation sequencing (NGS) on positive samples to enhance biosurveillance and monitor for variants. NCDC officials later credited the right technologies being in place before the pandemic struck, and having trained staff already operating at the Lugar Center, for its relatively strong initial COVID-19 responses as

133 National Center for Disease Control and Public Health, "Cooperative Biological Engagement Program Collaboration with DTRA," accessed November 8, 2022; Paata Imnadze, "NCDC / Lugar Center Capacities and Current Activities" *National Center for Disease Control and Public Health,* accessed November 8, 2022; U.S Department of Defense and Ministry of Defense of Georgia, "Concerning Cooperation in the Area of Prevention of Proliferation of Technology, Pathogens and Expertise Related to the Development of Biological Weapons" December 30, 2002.

compared to many other countries. As the pandemic persisted and evolved, the NCDC enhanced its use of NGS to better understand reinfections, variant trends, and other dynamics.[134]

Further, Georgia has served as a positive model for rapid data sharing during the pandemic, in particular richer data produced through its prioritization of using NGS over time. As of September 2022, the NCDC had uploaded 2,316 full genome sequences to GISAD and detected 97 variants.[135] The NCDC continues to integrate new tools into its national system as well, including bringing fieldable sequencers into use in fall 2022 and expanding wastewater sampling and analysis for early warning purposes.[136]

Beyond data sharing, Georgia's model for operations includes significant international collaboration. Its performance during COVID-19 was augmented by experts from U.S. WRAIR working in the Lugar Lab, as well as close collaboration with Germany's Bundeswehr Institute of Microbiology and numerous universities around the world. These mutually-beneficial collaborations span many public health, research, and defense organizations, woven together productively.[137]

---

134 Presentation by Gvantsa Chanturia, "Monitoring SARS-CoV-2 Variants in Georgia through NGS Technology," Biosafety Association of Central Asia and the Caucasus, Tbilisi, October 3–7, 2022.

135 Presentation by Gvantsa Chanturia, "Monitoring SARS-CoV-2 Variants in Georgia through NGS Technology," Biosafety Association of Central Asia and the Caucasus, Tbilisi, October 3–7, 2022.

136 Presentation by Gvantsa Chanturia, "Monitoring SARS-CoV-2 Variants in Georgia through NGS Technology," Biosafety Association of Central Asia and the Caucasus, Tbilisi, October 3–7, 2022.

137 U.S. Embassy in Georgia, "Lugar Center Supports Georgian NCDC on COVID-19 Response ," April 9, 2020; German Online Platform for Biosafety and Biosecurity, "IMB extends COVID-19 support for Georgia," May 8, 2020.

Kazakhstan

Much like Georgia, Kazakhstan has a long history of disease surveillance and epidemiological research. Although the Soviet Union diverted some of this expertise toward bioweapons development during the Cold War, subsequent collaboration among the Kazakhstan government, the United States, Russia, and others has helped the nation develop cutting-edge biosurveillance and early-warning capabilities.

HISTORICAL EFFORTS

Much of Kazakhstan's current disease surveillance architecture emerged from the Tsarist anti-plague system—a series of laboratories initially designed as a frontline outbreak monitoring network across former Soviet states. For decades, these labs studied high-risk naturally occurring diseases across Central Asia,[138] including Crimean Congo hemorrhagic fever, hantaviruses, tick-borne encephalitis, rickettsial diseases, and Q fever. Many of the central labs in this system eventually went on to function as hubs for the Soviet biological weapons program.

After the fall of the USSR, however, this network fell into disrepair. In response to this potentially catastrophic vacuum, the United States—via the Nunn-Lugar Cooperative Threat Reduction Program—stepped in to bolster Kazakhstan's capacity to detect emerging pathogens and secure hazardous biological materials.[139] Biosurveillance and disease early warning were central to this new collaborative relationship. Through the U.S. Defense Department's Biological Threat Reduction Program (BTRP),[140] for instance, the U.S. and

138 Lukas Peintner, et al., "Eight Years of Collaboration on Biosafety and Biosecurity Issues Between Kazakhstan and Germany as Part of the German Biosecurity Programme and the G7 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction," *Frontiers in Public Health* Vol. 9, 2021.

139 Kenneth B. Yeh et al. "A Case History in Cooperative Biological Research: Compendium of Studies and Program Analyses in Kazakhstan," *Tropical Medicine and Infectious Disease* Vol. 4, No. 4, 2019.

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

Kazakhstani governments constructed and improved several Biosafety Level 2 and 3 labs and implemented the Electronic Infectious Disease Surveillance System (EIDSS), a web-based surveillance reporting tool for both human and animal diseases. In total, BTRP has funded 30 biosurveillance-related projects and studies across Kazakhstan since 2003, as of this writing.[141]

TECHNICAL CAPACITY

Many Kazakhstani labs and institutions have benefited from this extensive cooperation. These include the Kazakh Scientific Center for Quarantine and Zoological Diseases (KSCQZD), the Uralsk Anti-Plague Station of the State Sanitary Epidemiological Surveillance Committee, the Research Institute of Biological Safety Problems, and the Central Reference Laboratory in Almaty (which eventually replaced KSCQZD in 2020).[142]

The comparatively new Central Reference Laboratory (CRL) is the centerpiece of U.S.-Kazakhstan bilateral biosurveillance and early warning collaboration. Constructed between 2015 and 2017 with $102 million in BTRP funding, it includes a BSL-3 lab and serves as Kazakhstan's national diagnostic reference laboratory and the country's leading diagnostic facility.[143] These functions were united into a single central lab site for the same cross-functional purposes described with regard to Georgia's equivalent lab; as such, it also maintains Kazakhstan's national collection of strains of especially dangerous pathogens from the Ministry of Health and Agriculture. The lab, jointly run by the latter two ministries alongside the Ministry of Education, also serves as a regional

141 Kenneth B. Yeh et al. "Building Scientific Capability and Reducing Biological Threats: The Effect of Three Cooperative Bio-Research Programs in Kazakhstan." *Frontiers in Public Health* Vol. 9, 2021.

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

143 Kenneth B. Yeh et al. "Significance of High-Containment Biological Laboratories Performing Work During the COVID-19 Pandemic: Biosafety Level-3 and -4 Labs." *Frontiers in Bioengineering and Biotechnology* Vol. 13, 2021.

research and training center for personnel from Armenia, Azerbaijan, Georgia, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, and Uzbekistan.[144]

There are other prominent bilateral and multilateral collaborations with Kazakhstan on biosecurity and early warning systems. A newly established joint EU-WHO fund of €10 million given to five Central Asian states, including Kazakhstan, aims to strengthen vaccine-preventable disease surveillance and enhance the use of digital solutions and digital health systems in the country.[145] In addition, an ongoing German-Kazakhstani partnership has actively worked to enhance biosafety and biosecurity in the country since 2013, including in disease surveillance and diagnostics. Through this partnership, Kazakhstan was able to expand its epidemiological surveillance and diagnostic systems to incorporate more endemic diseases and perform surveillance studies on the distribution of pathogen vectors in the country to better inform decision making.[146]

The CRL and other Kazakhstani labs played a central role in the region's response to COVID-19. In May 2020, for instance, the International Center for Vaccinology at the Kazakh National Agrarian Research University (KazNARU) and the National Scientific Center for Especially Dangerous Pathogens (NSCEDI) developed an early-stage vaccine candidate. The Kazakhstani government conducted vaccine studies at the CRL's biosafety level-3 lab. Known as QazVac, the government launched mass distribution of the vaccine in April 2021.[147]

144 Kenneth Yeh et al. "Significance of High-Containment Biological Laboratories Performing Work During the COVID-19 Pandemic: Biosafety Level-3 and -4 Labs." *Frontiers in Bioengineering and Biotechnology* Vol. 13, 2021.

145 European External Action Service. "European Union and WHO join forces for disease prevention and a stronger health care system in Kazakhstan," accessed October 26, 2022.

146 Lukas Peintner et al. "Eight Years of Collaboration on Biosafety and Biosecurity Issues Between Kazakhstan and Germany as Part of the German Biosecurity Programme and the G7 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction," *Frontiers in Public Health* Vol. 9, 2021.

147 Mikheyev P Auyezov O, Heinrich M. "Kazakhstan rolls out its own COVID-19 vaccine." *Reuters*, April 2021.

Separately, the CRL has also produced its own COVID-19 PCR tests for domestic use. According to local news coverage, the Kazakhstani Ministry of Health has started manufacturing these tests at scale, significantly reducing the need to rely on externally-developed PCR testing supplies.[148]

Finally, Kazakhstani facilities and labs have conducted extensive genomic sequencing of COVID-19 since the start of the pandemic. Beginning in August 2020, for instance, KazNARU and NSCEDI published the sequence of the spike protein from three different SARS-CoV-2 viruses isolated in Kazakhstan. The same institutions sequenced three further samples in November 2020 as part of Kazakhstan's testing and vaccine development program.

A Potential Regional Hub: The Biosurveillance Network of the Silk Road

Central Asia and the Caucuses boast comparatively advanced biosurveillance systems. Thanks partly to cooperative post-Cold War efforts to dismantle the former Soviet Union's network of biological weapons facilities, countries such as Kazakhstan, Georgia, and others possess significant capacity to detect and address emerging pathogens.

Crucially, the region also features several multinational collaborations focused on biosecurity issues. One of these, the Biosurveillance Network of the Silk Road,[149] has for years facilitated collaboration and expert exchanges among Armenia, Azerbaijan, Bulgaria, Georgia, Ukraine, and others. Launched in 2013, as a disease surveillance working group with support from the U.S. Defense Threat Reduction Agency,[150] the organization aims to create a sustainable early warning network across Central Asia and the Caucasus, with a

148 Long J. "Special Kazakh Biolabs Working Overtime to Fight COVID-19." *The Astana Times*, May 2020.

149 Biosurveillance Network of the Silk Road (BNSR) Annual Meeting, *Science and Technology Center in Ukraine*, September 27, 2022.

150 Biological Threat Reduction Program (BTRP): Bio-Surveillance Network of the Silk Road (BNSR), Stimson Center, accessed October 19, 2022.

focus on border areas. One of the network's major efforts, the "Cross-Border Platform," functions as a forum to improve disease surveillance capabilities amongst a series of country pairs, including Azerbaijan-Georgia, Kazakhstan-Uzbekistan, and Armenia-Georgia. Paired countries exchange monthly data with an emphasis on the "One Health" approach, which emphasizes the interconnection among human, animal, and environmental health.[151]

The BNSR played an early role in responding to the COVID-19 pandemic in Central Asia. Network members shared outbreak data, held consultations to exchange experience and best practices in responding to novel outbreaks, and organized webinars by subject-matter experts on epidemiological surveillance, response, detection, and laboratory diagnoses. The BNSR also worked with Georgia's Lugar Lab to sequence genomic information from new COVID-19 variants.

Moving forward, the international community and participating countries should view the BNSR as a viable candidate to serve as a regional early warning hub, given its head start working toward regional connectivity and information sharing. Some structural adjustments will need to be carried out: the BNSR is currently a nonprofit organization operated under the Georgian NCDC, though it is already in the process of becoming a fully independent entity. This will allow it to receive funding from partner and supporter nations, international organizations, and possibly philanthropic organizations.[152] Indeed, the BNSR may become a strong test case for how to leverage long-enduring investments in biosurveillance into a sustainable model for early warning across key regions.

151 Presentation by Ekaterina Jabidze, "The Biosurveillance Network of the Silk Road (BNSR)," Biosafety Association of Central Asia and the Caucasus, Tbilisi, October 3-7, 2022.

152 Presentation by Ekaterina Jabidze, "The Biosurveillance Network of the Silk Road (BNSR)," Biosafety Association of Central Asia and the Caucasus, Tbilisi, October 3-7, 2022; Co-author conversations in Tbilisi, October 2022.

Africa

Biosurveillance and early warning systems vary widely across African countries. Given the continent's diverse geography and economic/political circumstances, there is no "one-size-fits-all" approach to early warning or disease detection. Nevertheless, organizations such as Africa CDC and the WHO have devoted significant resources to the issue since well before the COVID-19 pandemic began. Africa CDC's Institute for Pathogen Genomics,[153] for instance, aims to improve continent-wide disease surveillance through an international network of genomic sequencing labs.

One of the continent's newest early warning systems is the Africa Pathogen Genomics Initiative[154]—an outgrowth of Africa CDC's broader monitoring efforts. Like Latin America's COVIGEN, the project aims to integrate pathogen genomics into disease surveillance, outbreak investigation, and pathogen control and prevention. The four-year collaboration[155] (begun in 2019) among Africa CDC, the U.S. CDC, the Bill and Melinda Gates Foundation, Microsoft, Illumina, and Oxford Nanopore Technologies is working to establish a continent-wide data-sharing platform, build a data library and sequencing repository, and train scientists across the continent to use next generation sequencing technologies. As of October 2022, PGI has published 120,178 COVID-19 sequences, as well as other high-consequence pathogens including Ebola and mpox, using a combination of next-generation and traditional sequencing tools that pull samples from national public health institutes.[156]

Another notable cross-national project with the potential to function as an early-warning system is the LabPlus Africa initiative,[157] sponsored by the EU

153 Institute of Pathogen Genomics (IPG), Africa CDC, accessed October 19, 2022.

154 US$100 Million Africa Pathogen Genomics Initiative to Boost Disease Surveillance and Emergency Response Capacity in Africa, Africa CDC, October 12, 2022.

155 Munyaradzi Makoni, Africa's $100-million Pathogen Genomics Initiative, December 2020.

156 Institute of Pathogen Genomics (IPG), Africa CDC, accessed October 19, 2022.

157 Project 85 - Strengthening Laboratory Capacacities in Africa Against COVID-19 and Other Epidemics: From Setup in Senegal to Scale Up in Africa (LABPLUS AFRICA), European Union, accessed October 19, 2022.

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

CBRN Center of Excellence. The project aims to scale up a network of mobile biosafety labs designed to quickly detect and identify pathogens from patients in hard-to-reach regions with limited or nonexistent healthcare infrastructure. The mobile labs will operate out of two regional hubs[158]—one in Kenya and the other in Senegal at the Institute Pasteur—and utilize next-generation sequencing technology to detect a variety of potential pathogens.[159]

The United States has several programs working with partners throughout Africa to bolster early warning capabilities, as well as help drive progress in biosafety and biosecurity. Over the past three years, BTRP has assisted in biological risk management activities in Nigeria, Tanzania, Uganda, and South Africa; trained epidemiologists throughout Cameroon, Ethiopia, Kenya, Senegal, and Tanzania; and assisted in the development and improvement of national laboratories in Cameroon, Ethiopia, Gabon, Liberia, and Senegal.[160] Furthermore, the United States is running two major sequencing and bioinformatics programs with African partners. The first sequencing consortium is run through DoD's overseas laboratory network and has run workshops

158 LABPLUS AFRICA, Praesens Care, accessed October 19, 2022.

159 Twist Pan-Viral Panel, Twist Bioscience, accessed October 19, 2022.

160 U.S Department of Defense, "Fiscal Year (FY) 2022 President's Budget: Justification for FY Project 85 - Strengthening Laboratory Capacacities in Africa Against COVID-19 and Other Epidemics: From Setup in Senegal to Scale Up in Africa (LABPLUS AFRICA)2022," Volume 1, Part 2 of 2, May 2021.

in Kenya to support both defense health and public health efforts in the region.[161] Additionally, the National Institutes of Health has partnered with the African Society of Human Genetics and the Wellcome Trust to form the Human Heredity and Health in Africa Initiative.[162] The initiative has funded over 50 projects throughout the continent aimed to bolster Africa's biobanks and research capacity to gain insight into variation across the human genome, addressing Africa's historical underrepresentation in genomic research.[163] These partnerships are critical to fostering innovation in the region and led to significant sequencing efforts including genomic research during the 2013-2016 West Africa Ebola Outbreak and detection of the index case of SARS-CoV-2 in Nigeria.[164]

In close coordination and collaboration with Africa CDC and the WHO, the G7-led Global Partnership Against the Spread of Weapons and Materials of Mass Destruction has established the Africa Signature Initiative.[165] The program seeks to bolster biosafety and biosecurity across the continent by partnering with key stakeholders such as Africa CDC, national ministries and public health labs, and the Global Partnership. One such effort is the Grand Challenge for Sustainable Laboratories, supported by Global Affairs Canada and the World Organisation for Animal Health, seeking innovative approaches to design safe laboratories to conduct infectious disease research in resource-limited settings.[166] Another area of emphasis within the signature initiative is to strengthen international cooperation, including the Biological Weapons Convention.

161 Irina Maljkovic Berry et al. "A Department of Defense Laboratory Consortium Approach to Next Generation Sequencing and Bioinformatics Training for Infectious Disease Surveillance in Kenya," *Frontier in Genetics* Vol. 11, 2020.

162 Fogarty International Center, "Human Heredity and Health in Africa (H3Africa) at NIH," *NIH,* October 14, 2022.

163 Paul Adepoju, "Tackling Africa's underrepresentation in genomics studies," *Nature Africa,* April 5, 2022.

164 Fogarty International Center, "Former Fogarty grantee leads COVID-19 genomics work in Africa," *NIH,* May, 2020.

165 Global Partnership, "Signature Initiative to Mitigate Biological Threats in Africa," accessed October 28, 2022.

166 Keith Hamilton, Jennifer Lasley, David R Harper, "Improving sustainability to avoid laboratory disasters," *OIE Bulletin,* June 2018.

One of the Africa Signature Initiative's largest efforts is to assist in the development of sustained pathogen early warning across the African continent. In addition to engaging in dialogue over subject matter expertise, one of the essential goals of this initiative is to build the political will of the leaders, including Ministers of Health and Defense, to sustain pathogen early warning in their respective nations.

One of the key aspects of building systems of sustainable pathogen early warning programs across the African continent is identifying the needs and infrastructure to conduct biosurveillance activities at the local, national, and regional levels. Pathogen early warning systems will need to account for migration patterns, porous borders, and the mixture of governmental resourcing throughout the 54 countries and disputed territories across the African continent.

Key investments should include local-level capabilities to monitor the emergence of known pathogens in at-risk communities. This will include bolstering laboratory capacities of equipment such as enzyme-linked immunosorbent assays and PCR testing—traditional laboratory equipment that can be scaled and modified as needed.

National and regional centers of excellence should be established and should invest in more robust tools, such as massively multiplexed techniques that are able to detect novel pathogens across multiple sample sources over the next five years. Platforms like CRISPR-based detection technology and metagenomic sequencing will enable regions to monitor the emergence of novel pathogens and provide feedback to the local level to increase surveillance of new pathogens of interest. The National Institute for Communicable Diseases in South Africa, Africa CDC, and the Global Partnership are working on establishing a regional center of excellence for diagnostic detection that may be further expanded for broader early warning purposes.[167]

Bolstering the capacity of resource-limited and remote settings across the continent will be another critical aspect of establishing true early detection

167 Author conversations with multiple subject matter experts during the Global Partnership Biological Security Working Group Meeting, October 6, 2022.

components across Africa. Innovative approaches such as the drone delivery networks used to transport test kits and samples throughout Rwanda, Ghana, and Nigeria offer one approach to bolstering pathogen early warning integration across sample sets and data across the system.[168] For conducting sentinel surveillance in austere environments, field-deployable platforms paired with satellite internet capabilities enable remote lab work with real-time data sharing.[169] Where applicable, self-reporting signs of potential disease among households, livestock, crops, and wildlife via mobile applications can assist with implementing One Health approaches to pathogen early warning.

In addition to targeting agile detection platforms that fit the needs of the user, the success of sustained pathogen early warning systems will depend on the humans making the decisions. One key will be establishing a digital surveillance network that integrates the data streams across the detection and diagnostic platforms. A trained team of computer programmers, data scientists, and infectious diseases experts will be essential to build a system for producing reporting mechanisms and data visualization tools that enables actionable infectious disease intelligence for decision makers to analyze.[170]

168 Alexander Onukwue, "Zipline is launching its drone delivery services under "difficult" conditions in Nigeria," Quartz Africa, June 3, 2022.

169 Stefan Prost, "What if you could take your lab in a backpack to explore life on Earth?," Nature Protocols, April 11, 2022.

170 Africa CDC, "African researchers lead scientific coalition developing surveillance system for detecting emerging pandemics in real-time," May 11, 2020.

EBOLA

Historically, the Ebola virus was one of many infectious disease threats that was neglected by most of the world. Its endemic region is limited to East-Central and West Africa.[171] In the few dozen Ebola outbreaks that have been tracked since the 1970s, most cases had limited geographic reach and spread.[172] These factors contributed to limited investments by most actors in improving capabilities for detecting and responding to Ebola outbreaks.

For many years, defense organizations in several nations formed a major exception to this challenge: in addition to needing to protect personnel in geographies where they might be exposed to hemorrhagic diseases, Ebola was one of many pathogens that were part of the Soviet Union's biological weapons program, which included work seeking to manipulate the virus and enhance its lethality.[173] As such, the U.S. Department of Defense (DoD) has been a major driver of research and development for detecting and defending against this infectious disease threat, extending to its work in advancing biosurveillance and improving the tools available to diagnose cases.

This dangerous combination of Ebola-related threats contributed to a unique moment in the history of collaboration across defense and civilian organizations in understanding and addressing emerging disease threats. A deadly Ebola outbreak emerged in West Africa in December 2013, was officially reported by the World Health Organization in March 2014, and declared over by the WHO in June 2016. The reported casualties included 28,646 cases and 11,323 deaths[174]—and it was widely agreed that the toll could have climbed significantly had it not been for a robust international response to halt its transmission.

That response included significant coordination among a range of actors, in support of the governments of Guinea, Liberia and Sierra Leone.[175] This naturally included the WHO and health providers such as Doctors Without Borders, though early in the outbreak the rising rate of infections made clear that more would need to be done to augment their extraordinary efforts. Private foundations and volunteers from around the world jumped in, as did defense agencies of countries

171 Sima Rugarabamu et al. "Forty-two years of responding to Ebola virus outbreaks in Sub-Saharan Africa: a review," *BMJ Global Health* Vol. 5, 2020.

172 Centers for Disease Control and Prevention, "Ebola Virus Disease Distribution Map: Cases of Ebola Virus Disease in Africa Since 1976," Updated June 21, 2021.

173 Joby Warrick, "Ebola crisis rekindles concerns about secret research in Russian military labs," *Washington Post,* October 24, 2014.

174 Centers for Disease Control and Prevention, "Ebola Virus Disease Distribution Map: Cases of Ebola Virus Disease in Africa Since 1976," Updated June 21, 2021.

175

that had done Ebola-focused work. Contributions by the U.S. Department of Defense ranged from logistical support for moving people and supplies to providing diagnostic and surveillance tools (add a bit of detail if we can).[176]

As several UK experts have described, this Ebola outbreak was also "one of the first instances of real-time sequencing being used in an acute setting to enhance outbreak understanding," including its uses in understanding clusters and transmission chains, and analyzing whether this multi-country outbreak stemmed from different zoonotic spillover events.[177] The sequencing capacities used for these purposes included those established through prior health- and biodefense-focused collaborations.

DoD programs have also played a role in tracking and responding to Uganda's current Ebola outbreak. The epidemic, centered in the western and central part of the country, began in September 2022. Ugandan authorities have thus far reported 64 confirmed cases, with nearly 25 fatalities as of mid-October.[178]

U.S. assistance to the Ugandan government has taken several forms. Most immediately, Washington has supplied Remdesivir, a broad-spectrum antiviral drug, monoclonal antibodies, and other trial medications used to treat infected health workers.[179] Perhaps more consequentially, however, DoD's longer-term investments in Ugandan public health infrastructure have also helped Kampala identify and quickly respond to the epidemic. Several infected health workers, for instance, were treated at the Joint Mobile Emerging Disease Intervention Clinical Capability (JMEDICC) center, a joint U.S. and Ugandan-run clinic housed at the Fort Portal Regional Referral Hospital.

JMEDICC was initially established in 2016 by the Ugandan government and DoD in response to lessons learned during the 2014 West Africa Ebola outbreak.[180] The center's primary objective is to build capacity in Uganda to conduct clinical trials during high-consequence pathogen outbreaks, including Ebola. For early warning purposes, the center also has access to equipment from the Joint Program Executive Office for Chemical, Biological, and Radiological Defense, such as

176 U.S. Department of Defense, "DoD Brings Unique Capabilities to Ebola Response Mission, Official Says," November 12, 2014.

177 Cordelia E. M. Coltart et al. "The Ebola Outbreak, 2013–2016: Old Lessons for New Epidemics," *Philosophical transactions of the Royal Society of London* Vol. 372, No. 1721, 2017.

178 European Centre for Disease Prevention and Control, Ebola outbreak in Uganda, as of 21 October 2022, November 2, 2022.

179 Steenhuysen J. "U.S. sends experimental antibody, antiviral drug to Uganda for Ebola outbreak," *Reuters*. October 2022.

180 Prossy Naluyima et al. "The Joint Mobile Emerging Disease Clinical CApability (JMEDICC) laboratory approach: Capabilities for high-consequence pathogen clinical research," *Neglected Tropical Diseases* Vol. 13, No. 12, 2019.

diagnostic tools that can be used to rapidly identify the Ebola virus in suspected cases and sequence samples to track an outbreak's spread.[181]

Center personnel, including a full-time team of 22 clinical, laboratory, and logistics staff (as of 2019), track potential outbreaks, develop clinical trial protocols, train on increasingly complex outbreak and biosecurity scenarios, and identify strategies to combat sepsis in austere environments.[182] In the event of an outbreak, JMEDICC's emphasis on long-term collaborative training is meant to facilitate improved patient care and the development of new therapeutic drugs.

Thus far, JMEDICC has served this purpose well. During the 2018-2019 eastern Democratic Republic of Congo Ebola outbreak, for example, Uganda faced at least two imported case clusters.[183] Due to relatively high levels of training and rapid-response capacity, however, neither led to sustained in-country transmission. Uganda has been similarly effective during the current outbreak. Although cases continue to rise modestly, authorities have largely managed to contain Ebola's spread. Among many lessons from this experience, it is clear that this is an example of past investments that tie early warning to action that should be sustained and built upon.

Unfortunately, this is not yet the trajectory in motion. Despite its successes, the Pentagon's Defense-Wide Review eliminated JMEDICC's U.S. funding beginning in fiscal year 2021.[184] Although the facility maintains some capacity, as demonstrated by its response during the recent outbreak, funding cuts have reduced its capabilities. If this type of work in Africa is not restored, it will have negative consequences for the region as well as for DoD: less readiness for defense personnel who need to operate in the region, weakened ties between the pathogen early warning developing on the continent and defense early warning and response needs, and ultimately less experience in all aspects of addressing types of diseases that are largely endemic on the African continent but that may become serious threats in future, deliberate threats, accidents, or naturally occurring outbreaks.

181 JPEO-CBRND, "JPEO-CBRND Supports International Partners in Congo Ebola Outbreak," accessed November 1, 2022.

182 JPEO-CBRND, "JPEO-CBRND Supports International Partners in Congo Ebola Outbreak," accessed November 1, 2022.

183 Christina Potter et al. "Retrospective identification of key activities in Uganda's preparedness measures related to the 2018-2020 EVD outbreak in eastern DRC utilizing a framework evaluation tool," *Global Public Health* Vol. 2, No. 5, 2022.

184 Department of Defense Fiscal Year (FY) 2022 Budget Estimates, *Chemical and Biological Defense Program*, May 2021.

Southeast Asia

Southeast Asia is both a strategically important region and one that carries major biological risks. It is a global hotspot for the emergence of novel pathogens due to its high natural disaster risks, exposure to climate change-related shifts in disease patterns, wildlife trade and consumption, high density of livestock, population exposure to wet markets, and other factors. Thus, the propensity for outbreaks to emerge from pathogens such as highly pathogenic avian influenza is increased in the region and requires active surveillance.[185] It is also a region that has grappled with numerous terrorist and insurgent groups over time, including some that have shown interest in unconventional weapons. In Indonesia, for example, pro-Islamic State groups have attempted to extract toxins from plant materials to make bioweapons to target police stations and places of worship, demonstrating how accessible materials for biological weapons can be.[186]

Similar to the regions highlighted above, many years of capacity-building in Southeast Asia have contributed to a good foundation on which to build regional pathogen early warning. Moreover, it is likely to be a testing ground for moving early warning forward in ways that remain responsible regarding biosafety and biosecurity, as described below.

Capacities Within Countries

Countries within the region have developed event-based surveillance systems in order to detect and respond to potential outbreaks quicker and more effectively. Vietnam, for example, utilizes reports from health workers as well as community members such as teachers and farmers who are taught how to recognize cases or clusters of priority diseases which was crucial during

185 Erjia Ge et al. "Using Knowledge Fusion to Analyze Avian Influenza H5N1 in East and Southeast Asia," *PLoS One* Vol. 7, No. 5, 2012.

186 V. Arianti, "Biological Terrorism in Indonesia," *The Diplomat,* November 20, 2019.

the pandemic.[187] Thailand maintains the Participatory One Health Digital Disease Detection (PODD) surveillance program by relying on regular reporting from volunteers on potential outbreaks from animals or humans through a mobile application which can be followed-up on with lab testing.[188]

These methods alone, however, are insufficient and not specific enough to detect novel emerging pathogens. COVID-19 has allowed the region to expand and enhance its testing capacity including in genomic sequencing to detect new SARS-CoV-2 variants of concern. Eight of the eleven countries in the region are now performing genomic sequencing as of March 2022. However, whether the required capacity and funding for sequencing will be increased or sustained after the pandemic and whether testing will cover areas of concern such as wet markets, high density livestock, or urban areas, remains unclear.[189]

There is a good foundation on which to expand this work, if nations in Southeast Asia continue to invest—and particularly if the United States continues its biodefense and pandemic prevention relationships in the region, which should be a top priority.

Collaboration with Thailand stands as an early test of this. One of the first signs of biodefense cooperation's significant contributions to broader health security during the onset of the COVID-19 pandemic was when in January 2020, Chulalongkorn University in Thailand was the first to sequence COVID-19 outside of mainland China.[190] This occurred by use of the biosurveillance infrastructure built through BTRP. The U.S. Department of Defense has rightfully pointed to this example to showcase the importance of its work, yet BTRP cooperation and support for EIDSS in Thailand, as well as other countries in Southeast Asia, may unfortunately be coming to a close. While the United States cannot sustain other nations' capabilities in

187 U.S. Centers for Disease Control and Prevention, "Vietnam Update: Community-Based Surveillance Yields Results," August 7, 2017.

188 Ending Pandemics, "Participatory One Health Disease Detection," accessed 2022.

189 World Health Organization, "COVID-19 Pandemic: Testing Capacities Grow Manifold in WHO South-East Asia Region, Focus Now on Enhancing Genome Sequencing," March 23, 2022.

190 Vayl Oxford, *Testimony Presented before the Intelligence and Emerging Threats and Capabilities Subcommittee of the House Armed Services Committee*, October 2, 2020.

perpetuity, it would make strategic sense to allow good past investments to continue and facilitate a smooth transition and handover, especially at a time when biological risks are rising and when tensions in this specific region are rising even faster. U.S. defense leaders or their global health security counterparts should step in to ensure their investments in early warning capacities in places like Thailand are carried forward, or at the very least flag the issue for philanthropic organizations or other countries to consider stepping in with assistance to prevent backtracking.

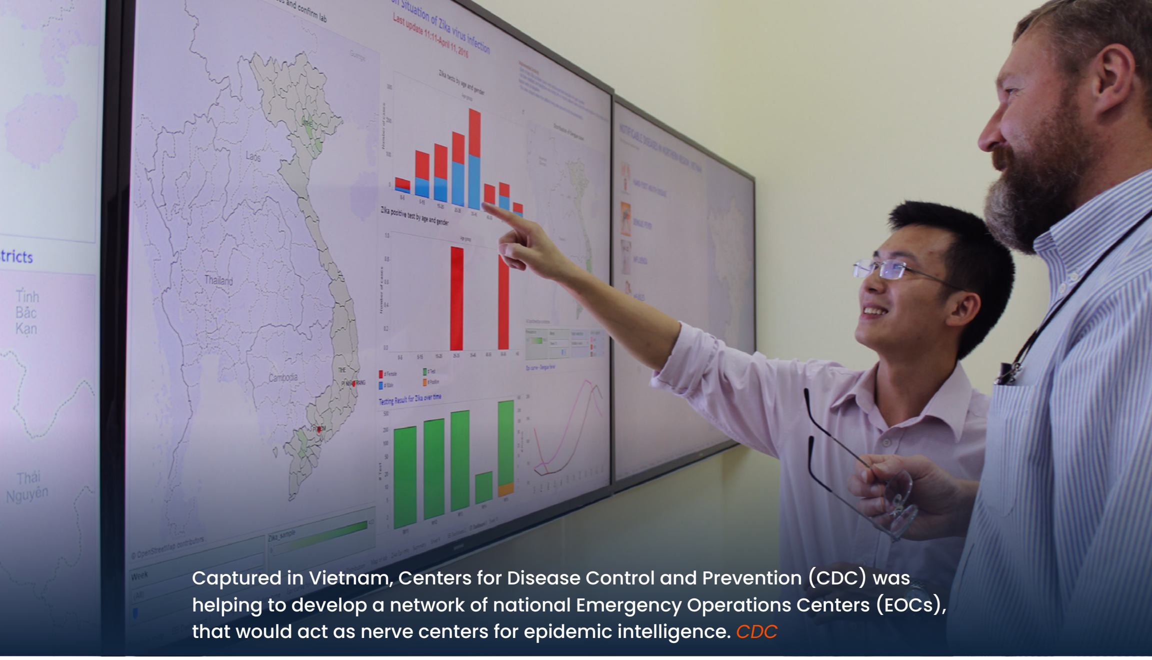
Another avenue through which the United States contributes to biosurveillance in the region is the USAMD-AFRIMS (Armed Forces Research Institute of Medical Sciences) lab and the Mekong-U.S Partnership Pathfinder Health Program. The USAMD-AFRIMS works with national governments and stakeholders to bolster biosecurity and emerging infectious disease surveillance in the region while the Mekong-U.S. Partnership Pathfinder Health Program focuses on helping communities prevent novel pathogen emergence and spread.[191]

Regional Collaboration

Southeast Asia is also home to numerous cooperative and information-sharing programs that can be augmented and built into improved regional early warning. On a regional level, six countries continue cross-border collaboration and surveillance through the Mekong Basin Disease Surveillance (MBDS) network. Established in 2001, the MBDS aims to strengthen national and regional capabilities in infectious disease surveillance and outbreak responses through inter-regional collaboration and information sharing.[192] The ongoing collaboration allows information sharing of lab results and event-based activities for emerging outbreaks of particular pathogens at cross border areas through a mobile application, as well as training on biosafety and biosecurity in those areas.

191 USAMD-AFRIMS. "Disease Surveillance," accessed November 1, 2022; Meking-US Partnership "Mekong-U.S. Partnership Pathfinder Health Program," accessed November 1, 2022.

192 Mekong Basin Disease Surveillance, "About Us," accessed October 18, 2022.



Captured in Vietnam, Centers for Disease Control and Prevention (CDC) was helping to develop a network of national Emergency Operations Centers (EOCs), that would act as nerve centers for epidemic intelligence. *CDC*

The region has also increasingly integrated the One Health approach into their surveillance systems. Established in 2011, it is home to the Southeast Asia One Health University Network (SEAOHUN) which increases One Health capacity for the prevention and detection of emerging threats in vulnerable areas through training and education.[193] SEAOHUN is funded by USAID's Strategies to prevent (STOP) Spillover program whose aim is to understand and reduce the risks for zoonotic virus spillover in the region through capacity building, and stakeholder engagement.[194] Currently, USAID is focused on implementing the STOP Spillover program in Cambodia and Vietnam by bolstering biosurveillance monitoring and reporting high-risk wildlife.[195] Other initiatives from the WHO bring a One Health approach and actively focus on preventing zoonoses such as from neglected parasitic diseases.[196]

Artificial Intelligence (AI) is playing an increasingly larger role in early warning systems and emerging disease surveillance.[197] BlueDot is a platform that

193 Southeast Asia One Health University Network, "Who We Are," accessed October 31, 2022.

194 Southeast Asia One Health University Network, "About STOP Spillover," accessed November 1, 2022.

195 STOP Spillover, "Vietnam Country Page," accessed November 1, 2022.

196 WHO Southeast Asia, "Facilitating One Health partnership for prevention and control of neglected parasitic zoonoses," accessed November 1, 2022.

197 Allam Zaheer, "The Rise of Machine Intelligence in the COVID-19 Pandemic and Its Impact on Health Policy. Surveying the Covid-19 Pandemic and its Implications," *AI*, July 24 2020.

sources data from over 10,000 official and media sources each day including population density, media reports, and climate conditions to identify hotspots and predict potential outbreaks. Notably, BlueDot was able to anticipate the outbreak of COVID-19 nine days before the outbreak was announced.[198] Using the BlueDot platform, the Association of Southeast Asian Nations (ASEAN) tracks and assesses infectious disease threats as well as predicting outbreaks to develop and implement mitigation strategies.[199] ASEAN aims to integrate the data into its newly established Center for Public Health Emergencies and Emerging diseases. The ability to track and predict outbreaks accurately can therefore be a powerful tool in an early warning system to identify and mitigate potential outbreaks from emerging pathogens.

Japan

Due to its geography and climate, Japan has to endure multiple, regular hazards such as floods, earthquakes, and tsunamis. The nation has also faced biological threats, including from the Aim Shinrikyo cult that carried out a terrorist attack with chemical weapons in 1995 and sought biological weapons as well. Hence, Japan has developed various early warning systems to help counter such threats including a relatively comprehensive biosurveillance system. In addition, Japan has heavily invested in technological and biomedical R&D for decades, putting its early warning systems in a strong position. Indeed, Japan's biosurveillance system as well as social behaviors such as masking contributed to a strong response against COVID-19 with only mild lockdowns imposed on the country accompanied by harsh border closures.

Japan's disease surveillance is amalgamated centrally at the National Institute of Infectious Diseases (NIID). The information of incidents of infectious diseases are collected from the country's prefectures to enable better decision

198 Isaac I Bogoch et al. "Pneumonia of Unknown Aetiology in Wuhan, China: Potential for International Spread Via Commercial Air Travel," *Journal of Travel Medicine* Vol. 27, No. 2, 2020.

199 ASEAN, "ASEAN BioDiaspora Virtual Center," accessed October 14, 2022.

making and rapid responses, with hospitals around the country obligated by law to report notifiable cases.[200] This not only involves cases for hospital patients, but incorporates a sentinel surveillance system from primary care as well as other methods of surveillance such as tracking school pupil absenteeism for some diseases. Japan also keeps track of imported cases by listing a presumptive country of import after diagnosis of certain diseases such as malaria. Moreover, when an epidemic or outbreak occurs, epidemiological investigations are carried out and information is exchanged with infectious disease surveillance organizations in other countries.

The COVID-19 pandemic has also accelerated Japan's historically laggard digitization of its health and surveillance systems compared to other developed countries. For example, Japan was able to deploy a contact tracing app shortly after the pandemic was declared and has started to shift toward the use of electronic health records.[201]

During the height of the Covid-19 pandemic, Japan was able to set up testing facilities for SARS-CoV-2 in four international airports to perform biosurveillance for imported SARS-CoV-2 cases. In addition, any positive cases were sent for whole genome sequencing to identify variants of concern before outbreaks occurred.[202] The rapid deployment of testing and sequencing at international airports proves the high ability for Japan to mobilize during pandemics or exposure to biological threats. However, in order to enhance their early warning systems, airport and pathogen agnostic testing through genome sequencing must be sustained and expanded to prepare for future threats. Similar to other developed countries, Japan also commenced wastewater surveillance, specifically for SARS-CoV-2, in order to forecast any outbreaks or spikes in cases.[203] However, testing is currently at a relatively small scale and

200 National Institute of Infectious Diseases, "Organizational Outline," accessed November 3, 2022.

201 Langley Esquire, "Going Digital: The Future of Healthcare in Japan," accessed November 4, 2022.

202 Suyoshi Sekizuka et al. "COVID-19 Genomic Surveillance Network in Japanese Airport Quarantine Stations in Japan, COVID-19," *Journal of Travel Medicine* Vol. 28, No. 2, 2021.

203 The Japan News. "Japan Eyes Sewage Monitoring Pilot Project to Understand Spread of Covid-19," June 3, 2022.

limited to certain prefectures and thus should be expanded geographically along with its ability to capture other known or emerging pathogens.

Japan has come a long way since the second World War where it was researching, developing, and deploying biological weapons, to being a signatory of the Biological Weapons Convention (BWC), working tirelessly for nonproliferation, and increasing biosecurity nationally and around the world. It is a member of the Australia Group where it limits the export and licensing of potential precursors to chemical or biological weapons, which is important for increasing international biosecurity. Moreover, Japan collaborates with countries in the Western Pacific on disease surveillance and information sharing through the WHO.

South Korea

South Korea has long been a leader in pandemic preparedness and pathogen early warning. Given its extensive history with infectious diseases and proximity to North Korea (which is widely believed to possess an offensive biological weapons program),[204] South Korea has invested heavily in public health and biodefense. Moreover, given the U.S. military presence on the Korean peninsula, Washington and Seoul have an extensive history of collaboration—both in public health and biodefense.

Today, South Korea operates one of the most advanced biosurveillance systems in the world. Given its advanced level of sophistication, its system represents an excellent candidate for a regional early-warning hub. Based around testing, tracing, and treating, the country's regime consists of two different, yet complementary systems. The first, or events-based surveillance, predicts disease outbreaks by aggregating a wide variety of information from public reports, news stories, rumors, or other intelligence. The second, or

---

204 U.S. Department of State, "Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments," April 2022.

indicator surveillance, reports and monitors clinical cases of specific diseases from hospitals and laboratories.[205]

Much of South Korea's technically sophisticated disease surveillance and early-warning architecture emerged after the 2015 MERS outbreak. Although the government eventually addressed the outbreak, Seoul's response was characterized by a number of failures. In the midst of a crisis, the government found itself without expert resources, infection control infrastructure, and an organized way of responding to medical emergencies.[206] The economy also suffered, with South Korea losing an estimated $2.6 billion in tourism revenue while spending nearly $1 billion on its response efforts.[207]

Building on its experience with MERS, South Korea was able to quickly respond to COVID-19. Soon after authorities detected the first infection within the country, the government focused heavily on quickly detecting new cases, containing them via isolation and quarantine measures, then treating sick patients as quickly as possible. When it came to detection and early warning in particular, South Korean authorities were able to rapidly and successfully build out high-capacity screening facilities and work with the private sector to ensure an adequate supply of tests.

Separate from its public health-focused efforts, South Korea also has a long history of pathogen early warning work for biodefense—especially in conjunction with the United States. Given North Korea's suspected biological weapons program, real-time pathogen detection and information sharing have long been priorities for alliance collaboration. Indeed, South Korea was home to some of the U.S. Department of Defense's earlier work to expand biosurveillance and extend rapid information sharing using web- and phone-based tools.

205 HyunJung Kim, "The Korean 3T Practice: New Biosurveillance Model Utilizing New Information Technology and Digital Tools," *JMIR Formative Research* Vol. 6, No. 5, 2022.

206 Myoung-don Oh et al. "Middle East respiratory syndrome; what we learned from the 2015 outbreak in the Republic of Korea," *The Korean Journal of Internal Medicine* Vol. 33, No. 2, 2018.

207 "Emerging COVID-19 success story: South Korea learned the lessons of MERS," *Our World in Data*, accessed November 3, 2022.

The South Korean and U.S. militaries conducted a series of joint exercises for several years designed to respond to potential biological events. Known as Able Response, the exercises were designed to coordinate inter-governmental responses to a series of naturally arising outbreaks and terrorist attacks, notably a theoretical anthrax attack targeting Seoul. Australia also participated in the Able Response program.[208] Separately, BTRP worked with the South Korean government to conduct another training exercise in 2019 known as Adaptive Shield, which was designed to assess the joint ability of U.S. and South Korean military and civilian authorities to respond to a novel pathogen outbreak.[209]

Finally, the United States and South Korean militaries have collaborated on a number of technical biodefense projects. One notable example is the Joint United States Forces Korea Portal and Integrated Threat Recognition program (JUPITR). JUPITR, run by the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) and supported by the U.S. Army Edgewood Chemical Biological Center (ECB) consists of three integrated components: the first is an information portal housing a library of identified biological substances accessible to authorized personnel. The second is a training program that sends ECB personnel to Korea to train U.S. forces on the peninsula. The final component is the so-called Integrated Base Defense—a sensor array that includes a pathogen-agnostic detection system designed to identify potential pathogens near military bases.[210] The sensor array includes acoustic, seismic, motion and other sensors with chemical and biological detectors. In a suspected biological attack, data from each instrument is assessed and synthesized to determine whether an attack occurred, and what type.

---

208 Seong Sun Kim et al. "Introduction of the Republic of Korea-the United States of America's Joint Exercise Against Biothreats in 2013: Able Response 13," *Osong Public Health and Res Perspectives* Vol. 4, No. 5, 2013.

209 Chaney A, "Detecting and Deterring Biological Threats, Then and Now" *Defense Threat Reduction Agency*, October 14, 2021.

210 ECBC Communications, "Improved biosurveillance capabilities for U.S. Forces Korea," *U.S. Army,* April 11, 2013.

Latin America

Latin America is emerging as a strong hub for early warning, based on past investments and a surge during COVID-19 that included regional collaboration and deployment of more advanced tools for pathogen-agnostic approaches. Positively, this regional cooperation is advancing in good coordination with the WHO and other actors.

Looking forward, the interface between public health and biodefense will be different in Latin America than in other regions. As it does not have deep histories tied to weapons of mass destruction threats—including uses in conflict or past biological weapons programs—it has not been a major focus for biodefense work to date. Still, this linkage comes into play in emergency responses, including as many Latin American nations are more commonly using defense forces for responding to disease outbreaks, natural disasters being fueled by climate change, and other transnational challenges including CBRN threats.[211]

Capacities Within Countries

States across Latin America will likely face several interrelated challenges related to biosurveillance and disease early warning over the coming decades. For one, climate change is primed to significantly alter weather patterns across the region. These shifts may alter the distribution of existing pathogens and strain underfunded health systems across the region. Separately, increased levels of deforestation and human settlement across the Amazon will inevitably increase human/animal interaction. New encounters of this type may increase the likelihood that novel pathogens enter human populations.

Latin American states are handling these challenges in a variety of different ways. Brazil, for instance, has long had a strong public health and biosurveillance track record—at least until the COVID-19 pandemic. Crucially, the country's designation of healthcare as a human right provides the basis for

211 OPCW, "CBRN experts from Latin America and the Caribbean expand chemical incident response capabilities," May 20, 2021.

a relatively comprehensive unified network of clinics and medical providers that can operate in a disease surveillance capacity. Brazilian health services, for instance, conduct extensive surveillance of dengue fever,[212] rabies,[213] tuberculosis and other diseases through the country's Notifiable Diseases Information System (SINAN).[214] SINAN, developed in 1993, provides real-time data on the number of confirmed cases of "nationally notifiable diseases." Data is collected from health facilities across the country.[215]

Separate from SINAN, Brazil also conducted extensive wastewater surveillance during the COVID-19 pandemic. Although the country's response to COVID-19 was hotly debated and became a national-level political issue, wastewater monitoring in several Brazilian cities has been helpful in identifying hotspots, providing data for early warning of new potential outbreaks, and conducting genomic sequencing for potential new variants of concern.[216] Brazil is also making progress toward integrating its broader pathogen surveillance efforts. In May 2022, for instance, the country held its first National Exhibition of Experiences of the Public Health Laboratory Network (EXPOLAB). The event brought together representatives from the country's 27 central public health laboratories, three national influenza centers, and 13 laboratories based in Brazil's border areas. The objective was to discuss how Brasilia might be able to strengthen its nationwide diagnostic and disease surveillance capacities.[217]

Elsewhere in Latin America, Mexico has also made some progress toward establishing effective biosurveillance and early warning systems. The country's

212 Marco Angelo et al. "Dengue Surveillance System in Brazil: A Qualitative Study in the Federal District," *International Journal of Environmental Research and Public Health* Vol. 17, No. 6, 2020.

213 Victor Bastos et al. "Challenge of Rabies Surveillance in the Eastern Amazon: The Need of a One Health Approach to Predict Rabies Spillover," *Frontiers in Public Health* Vol. 9, 2021.

214 Maril Souza Rocha et al."Notifiable Diseases Information System (SINAN): main features of tuberculosis notification and data analysis," *Epidemiol Serv Saude, Brasilia* Vol. 29, No. 1, 2020.

215 "Brazil Information System for Notifiable Diseases 2013," GHDx, accessed November 3, 2022.

216 Rodrigo de Freitas Bueno et al. "Wastewater-based epidemiology: A Brazilian SARS-COV-2 surveillance experience," *Journal of Environmental Chemical Engineering* Vol. 10, 2022.

217 "Brazil, PAHO, and WHO share experiences to improve diagnosis and genomic surveillance of the COVID-19 virus," *Pan American Health Organization,* May 2022.

Centro Virtual de Operaciones en Emergencias y Desastres (CVOED) operates a software system that provides support and communication capabilities to regions affected by crises, emergencies, or disasters. Although not exclusively pathogen focused, CVOED is able to collect and monitor information from a variety of sources to detect and respond to biological hazards that pose a risk to public health.[218]

Mexico also operates the National Epidemiological Surveillance System (SINAVE), which functions as the backbone of the state's capacity to detect biological threats and guide a national response. SINAVE grew out of Mexico's previous public health campaigns, including polio eradication efforts in the 1990s and the H1N1 pandemic in 2009. Today, SINAVE aggregates data from a network of 475 primary health care clinics and hospitals across the country, as well as the National Laboratory for Epidemiological Diagnostic and Reference. The latter institution leads a separate network of state laboratories.[219] SINAVE has the potential to act as a powerful early warning tool across Mexico, but its capacity is heavily dependent on funding, which has decreased consistently since its peak in 2011.[220]

Finally, Mexico and the United States jointly operate the Binational Border Infectious Disease Surveillance Program (BIDS). BIDS works with four U.S. states along the U.S.-Mexico border, as well as with the U.S.-Mexico Border Health Commission, to improve surveillance for infectious diseases of binational importance. Among other activities, BIDS supports monitoring efforts targeting respiratory illnesses including influenza and COVID-19 in border communities and among border-crossing populations. BIDS has also sponsored surveys at U.S.-Mexico land ports of entry to understand mobility patterns, alongside knowledge, attitudes, and practices related to COVID-19 and other pathogens.[221]

---

218 "Acerca de CVOED" *Gobierno de México,* accessed November 3, 2022.

219 Mariano Sánchez-Talanque et al. “Mexico's Response to COVID-19: A Case Study," UCSF Institute for Global Health Sciences, accessed November 3, 2022.

220 Mariano Sánchez-Talanquer et al. “Mexico's Response to COVID-19: A Case Study," UCSF Institute for Global Health Sciences, accessed November 3, 2022.

221 "Binational Border Infectious Disease Surveillance Program (BIDS)" Centers for Disease Control Prevention, accessed November 3, 2022.

Regional Collaboration

Like Central Asia, Latin America also features several efforts to establish cross-national disease surveillance and early-warning organizations. The region also has a longstanding laboratory network—including regional, national, and subnational institutions—with experience conducting genomic surveillance of influenza, foodborne disease outbreaks, and other respiratory viruses. Especially on the heels of COVID-19, many of these organizations expanded their work to include broader efforts to identify potential novel pathogens with pandemic or epidemic potential.

One of the larger Latin American cross-national surveillance efforts is the Pan American Health Organization's COVID-19 Genomic Surveillance Network of the Americas (COVIGEN).[222] The network was founded in 2020 to bolster connections between regional laboratories, improve national genetic sequencing capabilities, and develop a standardized COVID-19 sequencing process across 30 Latin American states and territories. Thus far, COVIGEN has focused primarily on detecting changes to COVID-19's genetic sequence that may influence the virus' ability to spread faster or cause more severe disease. The network relies on eight regional sequencing laboratories in Brazil, Chile, Colombia, Costa Rica, Mexico, Panama, Trinidad and Tobago, and the United States. As of October 2022, COVIGEN has published[223] 455,220 sequences—relying on a combination of next generation sequencing and traditional "first generation" sequencing methods.

Since 2021, COVIGEN has begun to pivot toward a broader disease surveillance and early warning mandate with a focus on genomic sequencing. The network recently published its Strategy on Regional Genomic Surveillance for Epidemic and Pandemic Preparedness and Response,[224] which focuses on "expanding and consolidating a regional genomic surveillance network"

222 COVID-19 Genomic Surveillance Regional Network, PAHO, accessed October 19, 2022.

223 COVID-19 Genomic Surveillance Regional Network, PAHO, accessed October 19, 2022.

224 Strategy on Regional Genomic Surveillance for Epidemic and Pandemic Preparedness and Response, PAHO, June 3, 2022.

dedicated to identifying emerging pathogens with pandemic potential. The proposal has four lines of effort:

- "expand and consolidate a regional genomic surveillance network for early detection and monitoring of emerging and existing pathogens beyond COVID-19;
- strengthen technical capacity for genomic sequencing;
- strengthen genomic data reporting and its integration with public health systems; and
- build capacity and define best practices for the use of genomic data in response to outbreaks, epidemics, and pandemics."[225]

Another notable collaborative regional disease surveillance effort centers on the U.S. Navy's Medical Research Unit Six (NAMRU 6), headquartered in Lima, Peru. Since 1983, the unit has teamed together with its Peruvian hosts and other Latin American partners to conduct biomedical research[226] on infectious diseases. The unit has several major focus areas, including research on diarrheal disease pathogens and assessing *Campylobacter*, Entero-toxigenic *E. coli* and *Shigella* candidate vaccines; identifying antibiotic-resistant bacteria in hospitals to recognize common resistance profiles; working together with partner militaries and civilian communities across South America on biosurveillance; evaluating candidate dengue virus DNA vaccines; and studying the insect disease vectors. Researchers from NAMRU-6 have also conducted studies[227] on the efficacy of self-administered rapid diagnostic tests to quickly detect and respond to emerging infectious disease outbreaks.

225 Strategy on Regional Genomic Surveillance for Epidemic and Pandemic Preparedness and Response, PAHO, June 3, 2022.

226 U.S. Embassy in Peru, Naval Medical Research Detachment, April 26, 2022.

227 Amy C. Morrison et al. "Potential for Community Based Surveillance of Febrile Diseases: Feasibility of Self-Administered Rapid Diagnostic Tests in Iquitos, Peru and Phnom Penh, Cambodia," *PLoS Negl Trop Dis* Vol. 15, No. 4, 2021.

Middle East

The Middle East boasts relatively few longstanding multilateral networks focused on pathogen surveillance and global health. Still, given the region's experience with endemic disease and history of biological weapons development, the U.S. government has dedicated significant resources to supporting local pathogen early warning systems on a bilateral basis. Most of these funds come from the Defense Threat Reduction Agency's (DTRA) Biological Threat Reduction Program (BTRP). BTRP, in turn, works primarily in Iraq, Jordan, and Gulf Cooperation Council (GCC) states—Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and the United Arab Emirates.

In Jordan, BTRP helped install[228] EIDSS—a nationwide software infrastructure designed to rapidly detect novel outbreaks. BTRP has also helped train Jordanian scientists, veterinarians, and public health workers to operate the system independently. Over the next three years, Washington is preparing[229] to phase out its external support and hand the system over to Jordanian authorities. Other Defense Department resources earmarked in 2022 are dedicated to improving the Jordanian government's ability to detect and report human and animal diseases caused by dangerous pathogens and build capacity to lead an effective regional biosurveillance network.

Existing BTRP funding for GCC states primarily focuses on building and evaluating existing regional capacity. Defense Department funding in fiscal year 2020, for instance, was earmarked for an ongoing assessment of current biosurveillance capabilities, alongside continuing technical support to enhance the council state's potential leadership roles in regional networks meant to counter the acquisition or use of dangerous biological materials.[230] More recent funding is slightly more forward-looking. For example, funds from BTRP's proposed 2023 budget are dedicated to developing partnerships meant to facilitate

228 Sustainment of Electronic Integrated Disease Surveillance System (EIDSS) and the Pathogen Asset Control System, Defense Threat Reduction Agency, August 6, 2020.

229 Fiscal Year 2023 Budget Estimates, Cooperative Threat Reduction Program, April 2022.

230 Fiscal Year 2021 Budget Estimates, Cooperative Threat Reduction Program, February 2022.

cross-border engagement on biorisk management, strengthen multilateral information sharing, and promote biosurveillance best practices.[231]

Given the United States' long-standing military role in Iraq, alongside Baghdad's legacy of biological and chemical weapons production, BTRP has a comparatively extensive presence in the country. Like Jordan, BTRP funds have gone toward setting up the EIDSS system. In 2017, Washington helped Baghdad install EIDSS in 49 sites[232] across the country. Other funds have gone toward laboratory renovations, equipment provision, and training Iraqi scientists. Fiscal year 2020 funds, moreover, went toward[233] biorisk and biosurveillance capacity building and electronic disease reporting efforts across Iraq. The latter support for biosurveillance efforts is set to continue until at least 2025.

The U.S. Department of Defense is not alone in building capacity in the region. The United Nations and NATO have also launched programs in the Middle East, including a joint partnership with Jordan to bolster Amman's capacity to deal with terrorist attacks involving biological, chemical, or nuclear weapons.[234] Initiated in 2019, the program has held a number of training sessions for Jordanian officials and first responders primarily focused on detection, response, and rapid decontamination.[235]

The U.S. Department of State has also contributed important work in the region. Through its Global Threat Reduction Program (GTR), for example, the Department of State has trained and equipped Iraqi counterterrorism and security forces to detect and respond to chemical and biological incidents. State Department GTR programs have also helped Egypt, Jordan, and Libya adopt security measures designed to prevent individuals or nonstate actors from

231 Fiscal Year 2023 Budget Estimates, Cooperative Threat Reduction Program, April 2022.

232 Department of Defense Countering Weapons of Mass Destruction Policy and Programs for Fiscal Year 2017, Homeland Security Digital Library, February 10, 2016.

233 Fiscal Year 2021 Budget Estimates, Cooperative Threat Reduction Program, February 2020.

234 NATO, "NATO and United Nations working together to strengthen Jordan's security and defence capacity against terrorist threats," March 5, 2019.

235 UN Office of Counter-Terrorism, "The First UN-NATO project trains Jordan officials at CEntre of Excellence in Europe," May 27, 2022.

acquiring weaponizable chemical, biological, or nuclear material and technology. Separately, the State Department's Export Control and Related Border Security (EXBS) program has funded efforts to help partner governments across the Middle East detect, interdict, and counter potentially weaponizable biological material. The EXBS program has also provided training for regional border security officials on border security, cargo, and passenger interdiction.

The U.S. CDC has a presence in Egypt, Jordan, and Saudi Arabia, where it works with those countries' ministries of health to improve emerging disease surveillance efforts—among other programs.[236] NAMRU-3 also collaborates with the CDC and has moved its base from Egypt to Italy as of 2020. It deploys both equipment and personnel to Africa and is focused on the long-term surveillance of enteric diseases, respiratory illnesses, acute febrile illness, disease vectors, and sexually transmitted infections as well as emerging infections like COVID-19.[237]

All of these engagement points offer opportunities to assess whether newer and more advanced tools, and training to use them, should be prioritized. This opportunity is enhanced by the fact that countries within the region are tooling up on their own accord in many cases. The United Arab Emirates, for instance, has been testing sewage from commercial aircraft for COVID-19 to determine whether any passengers were infectious.[238] Abu Dhabi also recently announced the launch of a wastewater monitoring lab designed to test for a variety of infectious diseases, parasites, pathogenic yeast, and fungi. According to the emirate's Department of Energy, the lab is meant to serve as an early warning system for potential contaminants and health threats.[239] Israel also has similar efforts underway.[240]

236 Centers for Disease Control and Prevention, "Where we work," accessed October 31, 2021.

237 Defense Visual Information Distribution Service. "NAMRU-3 tests us every day—and looks ahead to days after COVID," accessed November 2, 2022.

238 Freda Kreier, "The myriad ways sewage surveillance is helping fight COVID around the world," *Nature*, May 20, 2021.

239 Abu Dhabi Government Media Office, "Abu Dhabi Department of Energy Launches Wastewater Monitoring Lab," accessed October 31, 2022.

240 Kando, "Israel's Ministry of Health takes its COVID-19 wastewater project nationwide," January 4, 2022.

Unfortunately, multifaceted biological risks in the Middle East will remain part of the regional security environment for the foreseeable future. Concerns remain that the Syrian regime of Bashar al-Assad may continue to pursue weapons of mass destruction. According to the State Department's report on compliance with arms control, nonproliferation, and disarmament agreements and commitments, Iran has also engaged in dual-use activities with potential bioweapons application, including building a plant for pharmaceutical botulinum toxin production. Iranian military-associated universities and research centers have also apparently conducted bioweapons-relevant research on bioregulators and botulinum toxin.[241] Terrorist threats remain as well, and ISIS's attempt to develop chemical and biological weapons when it held significant territory was a striking example of how intentions and capabilities of such groups can continue to involve weapons of mass destruction.

241 U.S. Department of State, "2021 Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament AGreements and Commitments," April 15, 2021.

Australia and New Zealand

Australia and New Zealand also exemplify a strong blend of capabilities for addressing the full range of biological threats, including in early warning. Moreover, they work in collaboration with many other nations, have strong One Health visions for biosecurity, long histories of leadership in nonproliferation, and hold strong strategic relationships with the United States and many other nations.

Early Warning Capacities

Australia and New Zealand's aggressive national strategies to suppress SARS-CoV-2 during the pandemic included lockdowns, border closures, and contact tracing, contributing to both countries having among the lowest numbers of SARS-CoV-2 cases and deaths worldwide. In addition, both countries utilized and developed their surveillance systems during the pandemic, which could enhance their responses to future biothreats and outbreaks.

Australia has a robust and multi-faceted approach in its surveillance and early warning strategy which is outlined in its National Framework for Communicable Disease Control.[242] The framework involves collaboration across the federal, state, and local level for its response due to the government's more decentralized nature. To provide the required coordination and leadership for disease surveillance and prevention, the government established the Communicable Disease Network Australia (CDNA) where identifying trends and reporting detected outbreaks are among its objectives.[243] CDNA also provides advice and guidance for public health bodies on multiple national levels for detecting outbreaks, and publishes fortnightly reports from its National Notifiable Diseases Surveillance System on national trends for communicable diseases.

242 Australian Government. "National Framework for Communicable Disease Control," accessed October 18, 2022.

243 Australian Government. "Communicable Disease Network Australia," accessed October 18, 2022.

In addition, Australia deploys a sentinel surveillance system where a small group of health workers gather data on diseases and perform random testing within the community. As part of its sentinel surveillance system, the government established the Australian Sentinel Practices Research Network (ASPREN), a program where general practitioners (GPs) and nurses can report Influenza-like-illnesses (ILIs) and other conditions seen in general practice.[244] ASPREN functions by providing both syndromic surveillance for communicable diseases such as ILIs and gastroenteritis and testing for respiratory viruses in patients with ILIs.

The Australian government also performs genomic surveillance by working with the Communicable Diseases Genomic Network (CDGN).[245] Through its AusTrakka platform, CDGN performs genomic surveillance on different pathogens and integrates genomic epidemiological data to inform the Australian Department of Health's responses to new strains and variants.[246] Genomic data is also shared with New Zealand and can be shared internationally when needed. During the COVID-19 pandemic, CDGN expanded and utilized genomic surveillance to identify the emergence and growth of SARS-CoV-2 variants, with approximately 50% of total SARS-CoV-2 cases sequenced and uploaded as of February 2022.[247]

Both Australia and New Zealand commenced wastewater surveillance during the pandemic, although currently, it is primarily restricted to PCR tests for SARS-CoV-2, which is an inadequate tool for the detection of emerging pathogens.[248] However, the commencement of wastewater surveillance is

244 ASPREN website. "ASPREN: The National GP Surveillance Network," accessed October 18, 2022.

245 Communicable Diseases Genomics Network. "Australian Pathogen Genomics Program: Integrating pathogen genomics into public health," accessed October 18, 2022.

246 Communicable Diseases Genomics Network. "AusTrakka: Real-time Pathogen Genomics Surveillance," accessed October 18, 2022.

247 Tuyet Hoang et al. "AusTrakka: Fast-tracking Nationalized Genomics Surveillance in Response to the COVID-19 Pandemic," *Nature Communications* Vol. 13, No. 865, 2022.

248 New South Wales Government. "Covid-19 Sewage Surveillance Program," accessed October 18, 2022; and New Zealand Government. "Covid-19: Wastewater Testing," accessed October 18, 2022.

promising, as it may be a hook for both countries to expand their wastewater testing to other pathogens, provided that funding is sustained.

New Zealand has a similarly robust surveillance program for a list of notifiable diseases and it is primarily executed by the Institute of Environmental Science and Research (ESR). They have instituted a sentinel surveillance program to test for a plethora of pathogens in hospital-admitted patients as well as tracking respiratory diseases and gastroenteritis through data from GPs.[249]

New Zealand also performs genomic surveillance of different pathogens through ESR, including toxin-producing or antibiotic-resistant bacteria.[250] Furthermore, New Zealand expanded their genomic surveillance capacity during the pandemic in order to detect and track the transmission and emergence of novel SARS-CoV-2 variants, with the majority of confirmed cases sent for sequencing.[251]

Biodefense, Biosecurity, and Health Security Cooperation

Following the use of chemical weapons by Iraq in 1984, Australia led an initiative to establish the Australia Group in order to prevent the proliferation of chemical and biological weapons. Composed of 43 countries, the Australia Group limits export and licenses for some chemicals and biological agents that can lead to chemical or bioweapon development, in order to bolster adherence to the CWC and BWC.[252] The measures are intended to enhance biosecurity worldwide by licensing the export of biological agents and biotechnology equipment that could be utilized for the development of bioweapons. The United States, Australia, Canada, and the UK have also established a memorandum of understanding to improve their collective chemical, biological,

249 ESR website. "Influenza and Other Respiratory Virus Surveillance," accessed October 18, 2022.

250 Institute of Environment Science and Research. "Genomics and Next Generation Sequencing," accessed October 18, 2022.

251 Jemma L. Geoghegan et al. "Use of Genomics to Track Coronavirus Disease Outbreaks, New Zealand," *Emerging Infectious Diseases* Vol. 27, No. 5, 2021.

252 Nuclear Threat Initiative. "Australia Group," accessed November 1, 2021.

and radiological capabilities.[253] This includes the establishment of a working group to detect and address biological threats, thus strengthening biosecurity between the four countries.

Given their relatively robust approach, Australia and New Zealand have used their surveillance tools and expertise to amalgamate and track collected data on pathogens, and to subsequently mount early responses to prevent the development of outbreaks. In addition, both countries have forged strong international ties to collaboratively work to prevent, detect, and mitigate the emergence of novel pathogens through international coordination and information sharing.

253 U.S Department of Defense. "Chemical, Biological, and Radiological Memorandum of Understanding," accessed November 1, 2022.

Meetings of international bodies like the G7 Global Partnership have recently been the setting for discussions on how to best improve global pathogen early warning moving forward.

International Efforts & Global Connectivity

The international community continues to grapple with questions of whether and how regional, national, and sub-national efforts will come together to create what can be considered a global pathogen early warning system. To date, no organization is taking a role as the central lead for conducting and integrating pathogen early warning capabilities.

Over the past few years, several new organizations have made important steps towards addressing the need for advancing the international community's pathogen early warning capabilities, in addition to the WHO working to improve the interoperability of regional early warning efforts. Additionally, several non-government organizations have proposed new entities to address the critical gaps in global pathogen response, aiming to create mechanisms and organizations to provide expert analysis and public health support during the early days of an unknown infectious disease outbreak. These include the

WHO Hub,[254] the growth of its Biosecurity and Health Security Section,[255] a proposal to create a rapid response force,[256] and the formation of a new and independent organization to address global biological threats.[257]

World Health Organization Early Warning Advances

The WHO plays an important role in international surveillance, response, and coordination. Ensuring collaboration across regions and countries to provide a global network for information sharing and data collection is one of the most important missions for the WHO, which was only reinforced during the COVID-19 pandemic. To address the importance of early warning and increasing need, the WHO has initiated new endeavors, such as multi-disciplinary teams through Hubs, in addition to existing WHO efforts to ensure information sharing and IHR compliance. The coordination required for global health work requires consistent investment and monetary support, which historically has been a challenge for continuity of efforts and continuous improvement initiatives. Early warning efforts are one of many responsibilities and initiatives within the WHO and strengthening early warning on a global scale will require sustainable resources.

WHO Pandemic Hub in Berlin

The WHO is in the initial stage of building a cross-disciplinary team to better integrate epidemic intelligence systems. An element of the WHO's Health Emergencies Programme, the Hub for Pandemic and Epidemic Intelligence (referred to as "the Hub"), was officially launched in September of 2021. Almost

254 World Health Organization, "WHO Hub for Pandemic and Epidemic Intelligence," accessed November 14, 2022.

255 World Health Organization, "Strengthening the Global Health Security Interface," accessed November 14, 2022.

256 Angela Kane, Jaime M. Yassif, Chris Isaac, "Joint Assessment Mechanism to Determine Pandemic Origins," NTI, accessed November 2, 2022.

257 Ahmet Üzümcü, "International Response to Pandemics: Is there a need for a new international institution?," Council on Strategic Risks, April 27, 2020.

one year after beginning its operation in Berlin, the Hub continues to build its operational capacity as it staffs from the top down and develops its work portfolio.

The overarching mission of the Hub is to develop a network for global disease surveillance akin to the international air traffic control system, in that nations have their own national systems but they are able to effectively work safely together across borders.[258] The systems and operations built by the Hub will focus on connecting biosurveillance data sources and the local, national, and regional communities of practice. In doing so, the Hub aims to bolster the validity and interoperability of early warning data for the decision-makers on the ground to have the best information possible when making public health decisions for their communities. Whereas many speculated the Hub would serve as the central nervous system for collecting and analyzing the world's biosurveillance systems, instead it will be a team of experts building capacity through connectivity.

To help fulfill its mission, the Hub will seek out collaboration and interoperability across the board. Once fully operational, the Hub will aim to house 60 WHO employees along with 60 fellows on multi-year rotations in Berlin from a diverse set of partnering institutions.[259] With the member states being the primary stakeholder, the Hub will seek to bridge national biosurveillance programs, WHO Regional Hubs, and open-source data into a package of information that is clear and concise for the end-user. Early examples of the data connection to the visualization pipeline currently includes three major WHO projects: the Epidemic Intelligence from Open Sources (EIOS) Initiative,[260] the International Pathogen Surveillance Network,[261] and the Knowledge Representation and Reasoning project.[262]

---

258 Author Interview with Pierre Grant, WHO Hub for Pandemic and Epidemic Intelligence, October 7, 2022.

259 Author Interview with Pierre Grant, WHO Hub for Pandemic and Epidemic Intelligence, October 7, 2022.

260 WHO, "Epidemic Intelligence from Open Sources (EIOS)," accessed October 31, 2022.

261 Lisa L. Carter et al. "Global genomic surveillance strategy for pathogens with pandemic and epidemic potential 2022–2032," *Bull World Health Organ* Vol. 100, 2022.

262 WHO, "WHO Hub for Pandemic and Epidemic Intelligence," accessed October 31,2022.

As part of the effort to expand the connectivity to pathogen early warning data, the Hub is building on tools that are already in place while unlocking new analysis. One example of this is implementing radio transcription tools to expand early warning analysis in regions where radio is the dominant information relay due to limited access to the internet. Furthermore, the Hub intends to build guidelines for data standards and interoperability between regional partners. The goal of such activities is to ensure that laboratory networks are able to exchange genetic sequencing data and other pathogen-related data should an event require flexibility in laboratory networks.

Currently, the Hub is led by the former head of the Nigerian Centers for Disease Control, Dr. Chikwe Ihekweazu, and is staffed with 25 employees. As the Hub continues to build its operation, public and international stakeholder engagements will be an important aspect of the success of its mission. Understanding the unique constraints the WHO will face in bolstering regional connectivity of early warning frameworks and infectious disease reporting platforms will be important in understanding what gaps will persist in the global early warning landscape. While the Hub can make substantial contributions to progressing connectivity of early warning systems at the regional level by leveraging its regional hubs and willing international partners, it should not be viewed as an attempt for a global early warning system.

WHO BioHub Spiez Lab Launch

Upon the identification of a novel pathogen, swift information sharing is key to containing the outbreak and preventing further spread.[263] Emerging pathogens must be quickly sequenced and analyzed to determine the scope of the threat and to begin countermeasure development. However, countries in which pathogens are detected may not always have the resources to conduct this research, so they may elect to send their samples internationally to a more well-resourced laboratory. Even if the county where a pathogen originates does have sufficient resources, sharing samples internationally can allow for a

263 World Economic Forum, "Global cooperation is crucial for pathogen detection. The scientist who discovered the Omicron variant explains why," December 9, 2021.

greater volume of research to be conducted and for international partners to support response measures.

Historically, the sharing of pathogen samples and sequences has been done bilaterally and on an *ad hoc* basis, which can be inefficient as there is not a clearly established procedure or structure.[264] Additionally, some countries have been hesitant to share pathogen samples because they have not always reaped the benefits of research conducted using their samples—for instance, low-income countries that provide pathogen samples to high-income countries rarely receive access to the medical countermeasures that high-income countries develop using these samples.[265] While there are some mechanisms in place to address this, they are bureaucratically cumbersome and often do not have the desired outcome. Furthermore, researchers in low-income countries frequently are not credited for their work, and have their research contributions co-opted by researchers in high-income countries.

To help address these issues, WHO has established a new initiative called BioHub, which will designate a network of laboratories to serve as distribution and research hubs for pathogen samples.[266] Countries that detect a potentially novel pathogen or variant can safely and securely send their samples to one of the BioHub labs, which will conduct deep sequencing, analysis, and risk assessment that may not have been possible in the country where the pathogen originated. This research will then be shared with all WHO Member States, providing useful information to allow for the development of diagnostics and vaccines.

State and non-state entities can request pathogen samples from BioHub labs through an agreement that seeks to minimize biosecurity risks and ensures that ensuing research findings are widely accessible.[267] The Biohub system is intended

---

264 Jennifer Rigby, "Inside the super-secure Swiss lab trying to stop the next pandemic," *Reuters*, August 1, 2022.

265 National Academy of Medicine, National Academies of Sciences, Board on Global Health, "Pathogen Sharing for Influenza Vaccine Production," in *Countering the Pandemic Threat Through Global Coordination on Vaccines*: *The Influenza Imperative*, ed. Peter Sands and Janelle Winters (Washington D.C: National Academies Press, November 17, 2021), 61.

266 World Health Organization, "WHO BioHub."

267 World Health Organization, "Pilot Testing—WHO BioHub System—Stream 1," May 17, 2022.

to allow for a higher degree of structure and transparency, and has the potential to facilitate faster and safer pathogen sample sharing. As such, the BioHub will not only improve pandemic response, but may be a valuable biosecurity tool.[268]

The BioHub began a pilot phase in May 2021 by establishing a designated distribution and research facility at the Spiez Laboratory in Spiez, Switzerland.[269] Currently, the pilot phase is focusing solely on SARS-CoV-2 variants to test the feasibility of the system, but there are plans to expand the pilot to all pathogens in 2023. Several countries have voluntarily shared SARS-CoV–2 samples with the Spiez Lab, including Luxembourg, South Africa, and the United Kingdom.[270] In some cases, the program has proved efficient—the Spiez lab received samples of the Omicron variant 9 days after South Africa expressed it would like to send them. However, Peru, El Salvador, Thailand, and Egypt all signaled that they would like to send variants to Spiez Lab in early 2022, and all are still waiting for approval.[271] This is mainly because it is unclear who in each country can provide the necessary legal guarantees associated with sharing pathogen samples. WHO is working to address this issue and making efforts to smooth the process during the pilot phase.

The pilot program has also worked on promoting the sharing of biological materials with manufacturers in an effort to encourage more equitable development and distribution of medical products. The Council on Strategic Risks's research has indicated that ensuring countries receive the benefits they are promised in a fair manner will be a major driver of whether countries are more trusting and cooperative—or uncooperative and nationalistic—in biological threat reduction in the future.[272]

---

268 Lillian Parr, "The WHO BioHub: An Emerging Tool for Secure and Equitable Pathogen Sharing," Council on Strategic Risks, June 27, 2022.

269 World Health Organization, "WHO and Switzerland launch global BioHub for pathogen storage, sharing and analysis," May 24, 2021.

270 Aishwarya Tendolkar, "Pilot Biohub Facility at Spiez Enables Fast Sharing of SARS-CoV2 Variants," *Health Policy Watch*, March 3, 2022.

271 Jennifer Rigby, "Inside the super-secure Swiss lab trying to stop the next pandemic," *Reuters*, August 1, 2022.

272 Natasha E. Bajema et al. *Understanding the Threat of Biological Weapons in a World with COVID-19*, Council on Strategic Risks, February 2022.

The BioHub is still in its early stages, and a great deal of work must be done before the system is fully operational. However, it holds significant promise for improving states' abilities to quickly and effectively respond to health emergencies in an equitable and secure manner, and will be a valuable tool in a robust early warning system.

WHO Biosecurity and Health Security Interface

In addition to the creation of the Hub for Epidemic and Pandemic Intelligence, the WHO is looking to bolster its capability set within the Biosecurity and Health Security Protection division. The ambiguity surrounding the initial stages of the COVID-19 pandemic demonstrated a gap in the international community's framework to respond to an emerging biological incident of an unknown origin. The potential for future emerging outbreaks that are ambiguous if they are deliberate, accidental, or naturally occurring has caused the WHO to consider how it can bolster its response to such incidents.

One approach the Biosecurity and Health Security Protection division is taking to address this knowledge and response gap is developing the framework for future scenarios.[273] The intent is to add personnel with experience that intersects the technical side of emerging threats with the diplomatic knowledge of international frameworks like the Biological Weapons Convention. The new position within the unit will be to leverage the knowledge of public health intelligence and emerging threats into strategic dialogue across the WHO to build a guide for the action set the WHO should consider in its response to future ambiguous biological incidents.

In the event of a deliberate or ambiguous biological incident, the WHO's role would be to provide technical biosafety and biosecurity expertise on the ground and coordinate the public health response effort. The level of disinformation campaigns with COVID-19 and the accusations by the Russian Federation regarding the CTR laboratories in Ukraine and Georgia provide

273 Matthew Lim, *Speech Delivered to the 2nd Meeting, MX4 - Biological Weapons Convention Meetings of Experts*, September 6, 2021.

reason for disinformation around ambiguous and deliberate biological threats to be an area of emphasis by response organizations. One area the WHO will not play an active role in is the attribution or forensic analysis in the case of deliberate use of disease as a weapon.

In order to gain control over disease, organizations like the WHO are looking at several strategies around a group of experts to mount rapid response efforts. The global consensus is that the current state of readiness and response is not equipped to properly respond to and mitigate an ambiguous or deliberate biological threat.

Proposed Entities and Mechanisms

The WHO is not alone in recognizing the need for international mechanisms and response organization in light of the heightened risks posed by biological threats. While multiple proposed entities and mechanisms are in conceptual or early stages of development, leaders in the international community are eager to see how they gain support and momentum. It is possible that all of them will advance, covering current gaps in the international system in different ways. Additionally, each would contribute to and leverage early warning in different ways, leaving a need to further explore how each would fit into the picture of global pathogen early warning.

Nuclear Threat Initiative's Joint Assessment Mechanism

The Nuclear Threat Initiative (NTI) has recently proposed the foundation of a Joint Assessment Mechanism (JAM) that would create an international response team within the UN. NTI looked at the existing authorities to investigate outbreaks within the WHO and the Secretary-General's Mechanism (UNSGM) and saw a gap where uncertainty existed around the source of the virus as being outside of the public health remit of the WHO and the

UNSGM's authority to investigate deliberate biological weapons use.[274] The proposal is for the UN Secretary-General's Office to maintain a team of global health experts that can respond to emerging biological incidents within 48 hours under the authorization of the UN Secretary-General to establish the origin of the biological threat. If such a proposal moves forward, this would serve as an important consumer of early warning of emerging infectious disease events.

Gates Foundation GERM

The Gates Foundation is also looking to build out an organization focused on pandemic response. Housed within the WHO, the proposed Global Epidemic Response and Mobilization Team (GERM) would be tasked with managing future disease outbreaks.[275] The proposed organization's staff of 3,000 full-time epidemiologists, geneticists, vaccine developers, and rapid response workers would have the authority to declare a pandemic and coordinate the subsequent global response, including everything from drug development to border control measures.[276] During periods with no active outbreaks, the same team would help run exercises to prepare governments and multilateral organizations for future threats. Initially proposed in Bill Gates' recent book *How to Prevent the Next Pandemic*, GERM is still largely theoretical—although Gates has called for $1 billion per year in funding.[277] It may also be complicated to house such a structure within the WHO or other existing international organizations, given their broad mandates and funding dynamics.

274 Angela Kane, Jaime M. Yassif, Chris Isaac, "Joint Assessment Mechanism to Determine Pandemic Origins," NTI, accessed November 2, 2022.

275 Horton R, "Offline: Bill Gates and the fate of WHO," *The Lancet*, May 14, 2022.

276 Gates B, "Meet the GERM team," *GatesNotes*, April 30, 2022.

277 Nina Shapiro, "Bill Gates wants to help prevent next pandemic with 'best bargain you'll ever see,'" *The Seattle Times*, July 14, 2022.

International Biotech Organization

Another approach to addressing future risks of high-consequence pathogens and emerging outbreaks has been proposed by Council on Strategic Risks Senior Advisor, Ambassador Ahmet Üzümcü. Influenced by his experience as the former Director-General of the Organisation for the Prohibition of Chemical Weapons and the early response to COVID-19,[278] Ambassador Üzümcü has proposed establishing a new institution to address this threat, the International Biotech Organization (IBTO).[279] Functioning as an agile, independent, and impartial organization, the IBTO would be able to rapidly deploy its teams of technical experts to work on parallel missions, providing public health measures and medical advice to the local authorities on the ground, and simultaneously identifying the pathogen's origin. The vision is for the IBTO to be a public-private, multi-stakeholder enterprise that engages the biotech industry, the scientific community, and the philanthropic sector to guide and facilitate its efforts. Its mandate would encompass responding to any pathogen outbreak—deliberate, accidental, or natural—as an outbreak's origin would most likely be unknown and time is of the essence in taking prompt action to contain an outbreak.

The IBTO would be an independently operated and standing organization, composed of impartial subject matter experts and practitioners from across the international community. This operational model is an important distinction for several reasons. First, it would enable the IBTO to facilitate long-standing relationships with the international community. In risk-free periods, the IBTO team could run confidence-building exercises and focus on capacity building. By having a standing construct, IBTO rapid response teams would already be formed, trained, and have a functional performance level that can only come from working together as a team on a daily basis. Besides further honing team performance, this would also build familiarity and a level

278 Ahmet Üzümcü, "International Response to Pandemics: Is there a need for a new international institution?," Council on Strategic Risks, April 27, 2020.

279 John Moulton, Dan Regan, Ahmet Üzümcü, "Improving Response to Disease Outbreaks: Ambassador Üzümcü Makes the Case for New International Biotech Organization," Council on Strategic Risks, October 24, 2022.

of trust between the IBTO and national and local public health organizations around the world—crucial ingredients for success in effectively responding to an actual outbreak. Second, the organization would enable truly rapid deployment of its response teams. By being an independent organization, supported by the international community, it would be free of political interference that may prohibit rapid and robust operation by other global institutions. Additionally, it could immediately deploy its team of experts, as opposed to the extra time to call up a roster of international experts.

Another unique and crucial aspect is that the IBTO would be organized to respond to any outbreak, regardless of origin. Rather than having to characterize an outbreak as a suspected biological attack, an unintentional leak from a laboratory, a natural occurrence or being of unknown origin, an IBTO rapid response team could be launched if requested by the United Nations Secretary-General, Director-General of the World Health Organization, at the request of a member state along with the affected country accepting them, or by the Director of the IBTO to an emerging risk in a consenting country. This would help avoid delays in responding which could be needlessly generated by disagreement on the origins of an outbreak.

The concept of the IBTO was presented in October 2022 to the Biological Security Working Group of the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, a G-7 led, 31-country member international initiative aimed at preventing the proliferation of chemical, biological, radiological, and nuclear weapons and related materials. The Council on Strategic Risks continues to engage global partners and key stakeholders on the concept of the IBTO, and is looking forward to its development with Ambassador Üzümcü.

Entity X

These WHO and other entities may become key pieces for tying together early warning efforts across the globe. Yet a question still lingers: will a credible, neutral body emerge or be created within an existing organization that can serve as a master global pathogen early warning entity?

Over the past several years, many in the international community agreed on the strong need for this. Initial visions have not panned out for various reasons, including the continuing human and economic toll of handling a multi-year, global pandemic, alongside many smaller-scale but significant infectious disease outbreaks. Still, stakeholders should continue to consider possible pathways to developing such an entity.

Conclusion

Across the globe, nation states and international organizations have made important strides in bolstering pathogen early warning systems. The efforts laid out in this chapter have made significant progress in identifying gaps and forming regional consortiums and international partnerships to bolster biosurveillance efforts. This collaboration has proven a valuable way to address early warning needs within discrete locations. However, the looming question facing the international community is how to best integrate pathogen early warning systems into a cohesive, global whole. Bringing together an array of discrete early warning systems will take sustained attention and investment over the next decade.

Sample set for DNA genotyping and sequencing.

National Cancer Institute

V. Emerging Themes & Recommendations

CSR's objective in reviewing the current state of pathogen early warning is to focus global attention on this vital issue and, hopefully, drive movement toward a comprehensive system that can quickly identify and respond to new disease threats. This report has highlighted examples of technical progress, successful responses to emerging disease threats, and important shifts in U.S. and global policies. Still, although governments and international institutions have made headway, actors around the world urgently need to translate those advances into effective and lasting implementation.

Some of the most important near-term actions the United States can take include answering a series of questions outlined in this report. They include:

- **How will the CDC define the CFA's role in U.S. interagency coordination?** What role will CFA play in global early warning systems and what partnerships will it harness for this capacity?
- **How will DoD reorganize its biosurveillance and early warning programs**, a step that may result from the ongoing Biodefense Posture Review.
- **If the CFA and DoD's Global Emerging Infections Surveillance (GEIS) program continue ingesting data from around the world, will Executive Branch leaders and Congress require these systems to integrate some or all inputs?**

As it considers the preceding choices, the U.S. government should also incorporate the following recommendations into its decision-making processes. Successful pathogen early warning in the United States will require the following steps:

- A useful early-warning system must be able to identify a variety of pathogens, including high-consequence diseases, re-emerging strains, novel organisms, and meaningful genetic variations of

known pathogens. Such an operation must be **flexible, agile, and effective against any emerging threat, including those not included in the U.S. Select Agent List or Australia Group pathogens**. Although such lists will be important for specific biosurveillance efforts, pathogen early warning systems must move toward identifying any potential high-consequence pathogen, whether deliberate, accidental, or natural.

- **Successful pathogen early warning in the United States requires sufficient long-term funding.** Unlike past efforts that were often locked into decades-long contracting processes, new resources must be agile enough to accommodate rapid advances in technology. In order to achieve this goal, CSR has outlined a budget of $10 billion for biodefense and biosecurity and $10 billion for pandemic preparedness and global health security across DoD, HHS, and interagency over 10 years.[280]
- Government departments involved in developing an early warning system must **increase data connectivity and transparency**. Access to timely information is vital to mitigating the spread of any potential pathogen. The CFA can play a unique role in this system as a data air-traffic controller. One way to achieve this is for interagency teams to be co-located within the CFA, alongside detailees and other infectious disease experts. NSM-15's mandated annual exercise will be an important tool for identifying and implementing changes on this front and improving details to refine implementation to ensure early warning meaningfully improves biological threat risk reduction and responses.
- An effective early warning system will require **constant monitoring and routine evaluation through exercises and ongoing conversations about long-term strategy**. Such efforts are necessary to ensure that a future system meets the evolving needs of all government agencies and regions. To carry out this mission, government

280 William Beaver et al. *A Handbook for Ending Catastrophic Biological Risks*, Council on Strategic Risks, December 2021.

departments need to develop standardized evaluation and quality metrics. This systematized approach to program evaluation can provide a replicable way of comparing multiple early warning approaches while ensuring transparency and continuity.

- Within the next several years, DoD should **envision an ideal, pathogen-agnostic early warning system** to be developed at a minimum of two-three select bases, while advancing general-purpose plans for all defense facilities that can be tailored to fit unique needs.
- **Reinvigorate DoD's international partnership programs.** BTRP must also improve transparency around its programming and future plans given how early warning is evolving globally, to ensure other actors can assist with resourcing needs, and to effectively leverage early warning for deterrence.
- Across its international and domestic biosurveillance activities, DoD should implement **a systems approach** to ensure that multi-layered surveillance capabilities are connected to the integrated early warning system, providing feedback loops across all biosurveillance activities.
- The United States should **increase its contributions and collaboration with the G7 Global Partnership.** The Global Partnership is playing a key role in advancing pathogen early warning, bolstering biosafety, countering disinformation, and improving global compliance with international norms set within the Biological Weapons Convention.

With regard to the private sector:

- The U.S. government should **partner with private sector firms that have built their own COVID-19-based early warning systems**. Such partnerships can strengthen public health responses through information sharing and support the development of an agile and robust early warning system. Collaboration with private industry can also fill technical and operational gaps that exist within government.
- The U.S. government should foster an **active and dynamic relationship with the bioindustrial base.** The pace of progress

within the biotech industry requires a different approach than the traditional relationships that exist between government and the defense industry, which often move slowly. Across the interagency, U.S. officials should prioritize industry engagement opportunities, clear communication, and forms of technology development that incentivize private-sector participation. .

Although these initial recommendations focus primarily on U.S. policies and programs, a comprehensive early warning system necessitates global collaboration. The following recommendations are relevant to all nations and actors.

- States should **prioritize investments in pathogen-agnostic capabilities for pathogen early warning.** Although many states have invested heavily in biosurveillance and early-warning capacity over the past three years, these tools are often narrowly focused on tracking the spread and evolution of the SARS-CoV-2 virus. Going forward, governments need to ensure that early warning systems can detect any high-consequence pathogen. To counter future biothreats and enable rapid containment of novel and emerging pathogens, investments in early warning systems should aim to be massively multiplexed and/or pathogen agnostic.
- States must **invest in a multi-layered approach to pathogen early warning**. Developing surveillance methods that incorporate multiple indicators of biological events will be important to advance pathogen early warning. Data streams including transcribed radio broadcasts, social media trends, target enrichment and metagenomic NGS, and syndromic surveillance can provide the breadth and depth needed to detect emerging cases.
- Governments and international organizations must **work to improve early warning data interoperability and information sharing**. Regional and cross-border information sharing is an integral part of pathogen early warning, especially in areas with transient populations and porous borders. To this end, cross-border regions should increase their sharing of de-identified test results and

syndromic surveillance data. Regions should also pool resources to establish hubs dedicated to monitoring, providing expert guidance, and instituting more complex surveillance tools such as metagenomic sequencing. On the international level, the WHO Hub in Berlin should take the lead in developing an approach to standardizing infectious disease reporting and laboratory-based diagnostic test results.

- Wealthy states should **support community-based surveillance in resource-limited environments**. Early warning and surveillance systems are dynamic and complex, making them challenging to build in vulnerable communities that lack resources or capacity, such as low- and middle-income countries. More affluent actors can partner with those countries to supply them with the required resources, support capacity building, and forge partnerships to enhance their early warning systems. This will make states more resilient to future biothreats and subsequently strengthen global biosecurity, especially as factors such as climate change affect migration patterns and alter endemic disease prevalence.
- The global community needs to **develop incentives for reporting novel pathogens or emerging outbreaks.** Timely reporting of novel outbreaks and new variants of enduring outbreaks is vital for clamping down on the spread of disease. However, implications like travel restrictions and wildlife culling can often create a culture that disincentivizes vital reporting. Leveraging incentive structures, such as access to diagnostics, therapeutics, vaccines, and debt suspension measures,[281] should be expanded to promote pathogen early warning reporting. Better biosafety norms can be an implicitly valuable component of an early warning system. Incentivizing different states and actors to implement effective biosafety policies and report on pathogen zoonoses from wildlife and livestock or accidental lab leaks may aid the international community in detecting potential outbreaks earlier.

281 Esther Krofah et al. A Global Early Warning System for Pandemics: A Blueprint for Coordination, Milken Institute, March 2022.

- **Dual-use research areas of concern will need to be considered when expanding biosurveillance programs.** Private industry should bolster their cybersecurity efforts and generate plans for securing biosurveillance information to prevent malign actors from easily accessing data of dual-use concern as they continue to pursue the development of biological weapons.[282] Addressing the dual-use implications within the rapidly expanding biotechnology sector should be a significant area of emphasis as zoonotic spillover risks expand.

282 U.S. Department of State, "Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments," April 2022.

VI. **Conclusion**

Over the last three years, the COVID-19 pandemic has been the main driving force behind the adaptations and advancement of pathogen early warning systems across the globe. As such, the majority of new surveillance capabilities are targeted at the detection of COVID-19. In order to progress pathogen early warning, the driving force must be the detection of all potential high-consequence pathogens. The resurgence of Ebola, mpox, and polio has demonstrated the need for action in bolstering biosurveillance activities and striving for increased connectivity and feedback across systems.

Though there is significant progress, clear challenges remain. One of the most sweeping is that—despite recognized interest and need—no single entity has emerged to orchestrate and integrate how global pathogen early warning advances.

There is still a chance for a neutral, respected entity to fill this gap. However, progress cannot hinge on that. In the meantime, it is imperative to sustain the progress that has been made in response to the COVID-19 pandemic, and continue building national and regional capacities leveraging past investments as much as possible. In particular, this will require that the perceived seams between different disease threats and actors working to address them be dissolved once and for all.

For our part, CSR plans to continue working across key stakeholders in the global pathogen early community to bridge common interest and encourage stronger partnerships. This may take shape over a series of working groups to map the capabilities, interests, and critical gaps that exist within the governments, non-government organizations, philanthropic institutions, private industry, and the global biosecurity community to create a framework on how global pathogen early warning can advance. It is also clear that nongovernmental organizations, working with government and private sector actors,

may be best placed to create a roadmap to most effectively spread pathogen early warning capabilities.

The timeline for this work is pressing, given that some nations are already slowing or halting work to build on their past investments, no matter the positive impacts that work had. The world cannot afford another significant biological event—not in lives, nor in dollars. Continuing to build and spread pathogen early warning capacities is one of the clearest win-win choices the world can make now.

Annex

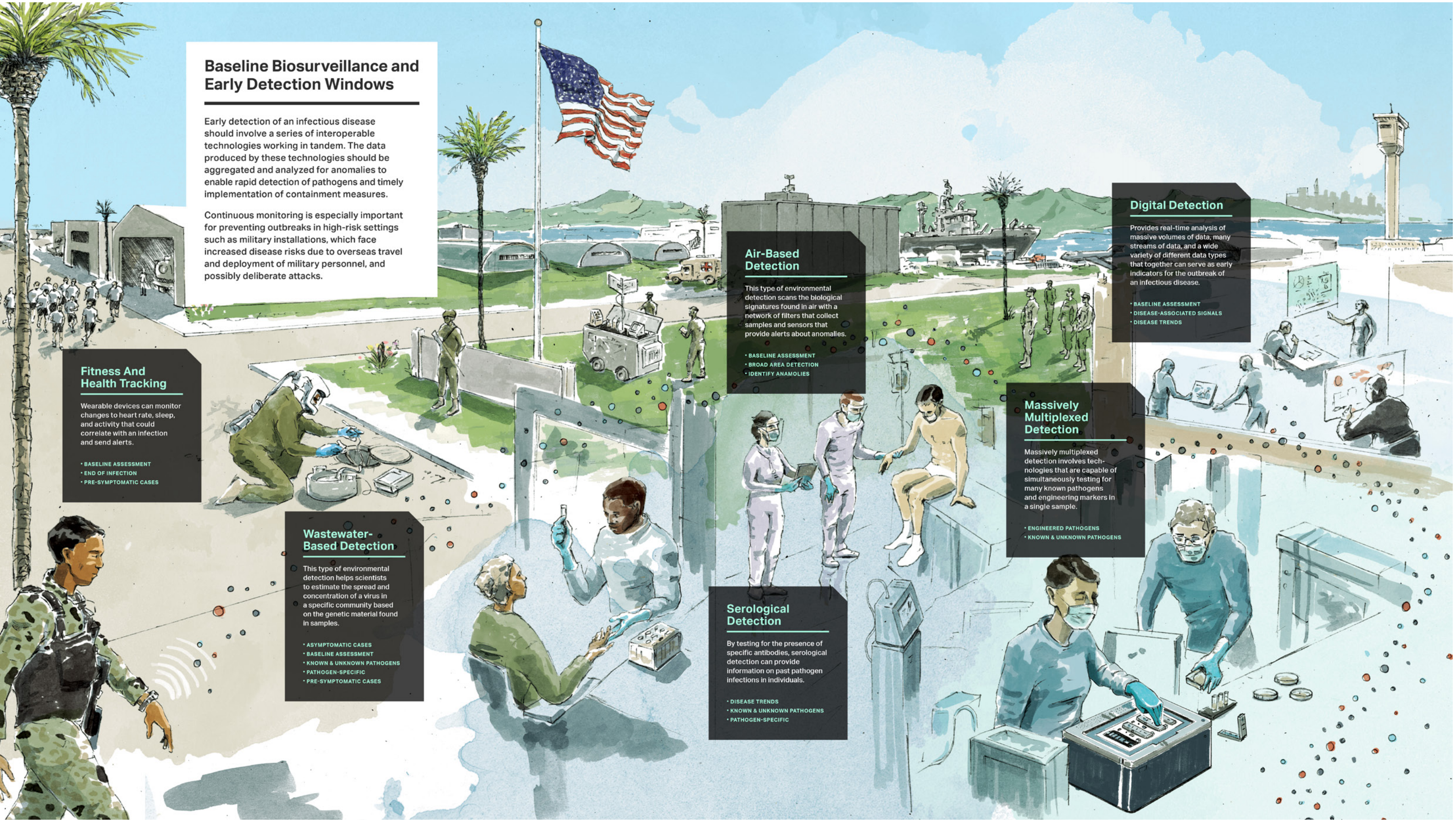
Previous work by CSR focused on identifying key biosurveillance capabilities and how a biological signal may trigger pathogen early warning systems. In doing so, Dr. Natasha Bajema of the Converging Risks Lab, an institute of the Council on Strategic Risks, and Brian G. Payne of aTON created these illustrations as a unique visual tool for understanding the scope of equipment, strategy, and people necessary for a successful biosurveillance network.

Two sets of illustrations are included in this annex, with each element expanded for accessibility.

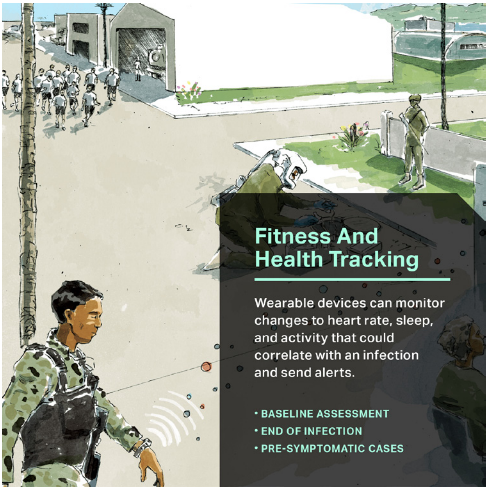
The first illustration explores critical biosurveillance capabilities and their interoperability in providing force health protection on a military installation.

The second illustration outlines the workflow of an infectious disease outbreak and how the biosurveillance network would be put into practice across the U.S. government.

For further viewing on electronic devices, the digital illustrations can be explored on the Council on Strategic Risks website.



Baseline Biosurveillance and Early Detection Windows
Early detection of an infectious disease should involve a series of interoperable technologies working in tandem. The data produced by these technologies should be aggregated and analyzed for anomalies to enable rapid detection of pathogens and timely implementation of containment measures.
Continuous monitoring is especially important for preventing outbreaks in high-risk settings such as military installations, which face increased disease risks due to overseas travel and deployment of military personnel, and possibly deliberate attacks.
Fitness And Health Tracking
Wearable devices can monitor changes to heart rate, sleep, and activity that could correlate with an infection and send alerts.
• BASELINE ASSESSMENT
• END OF INFECTION
• PRE-SYMPTOMATIC CASES
Wastewater-Based Detection
This type of environmental detection helps scientists to estimate the spread and concentration of a virus in a specific community based on the genetic material found in samples.
• ASYMPTOMATIC CASES
• BASELINE ASSESSMENT
• KNOWN & UNKNOWN PATHOGENS
• PATHOGEN-SPECIFIC
• PRE-SYMPTOMATIC CASES
Air-Based Detection
This type of environmental detection scans the biological signatures found in air with a network of filters that collect samples and sensors that provide alerts about anomalies.
• BASELINE ASSESSMENT
• BROAD AREA DETECTION
• IDENTIFY ANAMOLIES
Serological Detection
By testing for the presence of specific antibodies, serological detection can provide information on past pathogen infections in individuals.
• DISEASE TRENDS
• KNOWN & UNKNOWN PATHOGENS
• PATHOGEN-SPECIFIC
Massively Multiplexed Detection
Massively multiplexed detection involves technologies that are capable of simultaneously testing for many known pathogens and engineering markers in a single sample.
• ENGINEERED PATHOGENS
• KNOWN & UNKNOWN PATHOGENS
Digital Detection
Provides real-time analysis of massive volumes of data, many streams of data, and a wide variety of different data types that together can serve as early indicators for the outbreak of an infectious disease.
• BASELINE ASSESSMENT
• DISEASE-ASSOCIATED SIGNALS
• DISEASE TRENDS



Fitness And Health Tracking

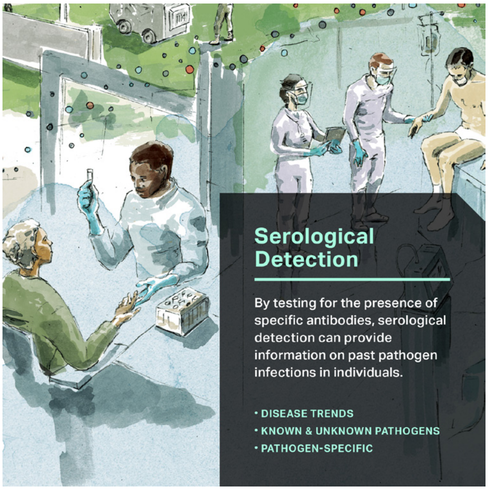
Wearable devices can monitor changes to heart rate, sleep, and activity that could correlate with an infection and send alerts.

- BASELINE ASSESSMENT
- END OF INFECTION
- PRE-SYMPTOMATIC CASES

Wastewater-Based Detection

This type of environmental detection helps scientists to estimate the spread and concentration of a virus in a specific community based on the genetic material found in samples.

- ASYMPTOMATIC CASES
- BASELINE ASSESSMENT
- KNOWN & UNKNOWN PATHOGENS
- PATHOGEN-SPECIFIC
- PRE-SYMPTOMATIC CASES



Serological Detection

By testing for the presence of specific antibodies, serological detection can provide information on past pathogen infections in individuals.

- DISEASE TRENDS
- KNOWN & UNKNOWN PATHOGENS
- PATHOGEN-SPECIFIC

Air-Based Detection

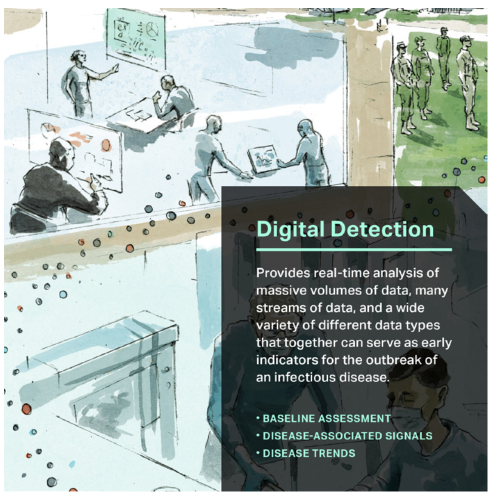
This type of environmental detection scans the biological signatures found in air with a network of filters that collect samples and sensors that provide alerts about anomalies.

- BASELINE ASSESSMENT
- BROAD AREA DETECTION
- IDENTIFY ANAMOLIES

Massively Multiplexed Detection

Massively multiplexed detection involves tech-nologies that are capable of simultaneously testing for many known pathogens and engineering markers in a single sample.

- ENGINEERED PATHOGENS
- KNOWN & UNKNOWN PATHOGENS



Digital Detection

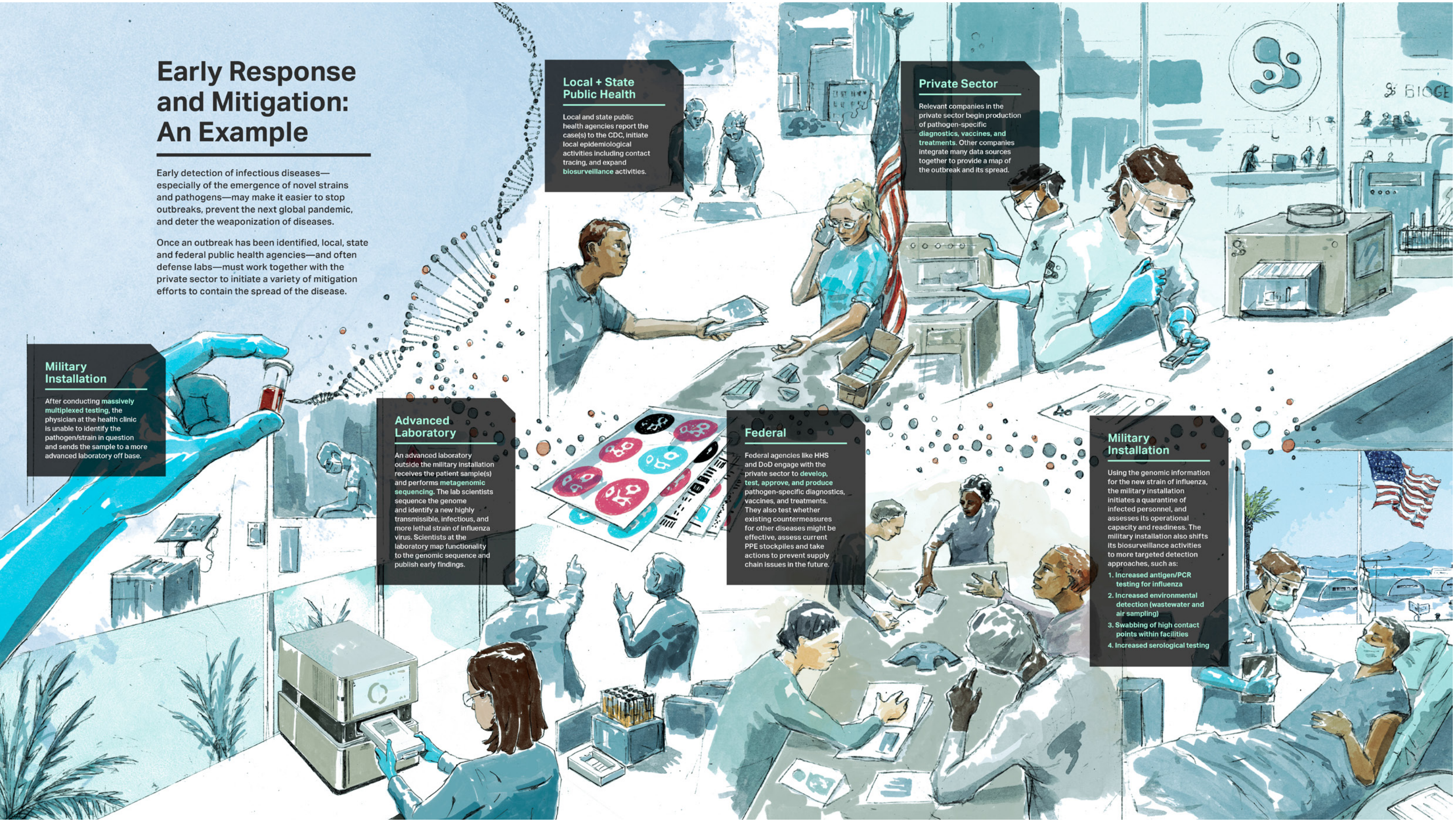
Provides real-time analysis of massive volumes of data, many streams of data, and a wide variety of different data types that together can serve as early indicators for the outbreak of an infectious disease.

- BASELINE ASSESSMENT
- DISEASE-ASSOCIATED SIGNALS
- DISEASE TRENDS

Early Response and Mitigation: An Example

Early detection of infectious diseases—especially of the emergence of novel strains and pathogens—may make it easier to stop outbreaks, prevent the next global pandemic, and deter the weaponization of diseases.

Once an outbreak has been identified, local, state and federal public health agencies—and often defense labs—must work together with the private sector to initiate a variety of mitigation efforts to contain the spread of the disease.



Military Installation

After conducting **massively multiplexed testing**, the physician at the health clinic is unable to identify the pathogen/strain in question and sends the sample to a more advanced laboratory off base.

Advanced Laboratory

An advanced laboratory outside the military installation receives the patient sample(s) and performs **metagenomic sequencing**. The lab scientists sequence the genome and identify a new highly transmissible, infectious, and more lethal strain of influenza virus. Scientists at the laboratory map functionality to the genomic sequence and publish early findings.

Local + State Public Health

Local and state public health agencies report the case(s) to the CDC, initiate local epidemiological activities including contact tracing, and expand **biosurveillance** activities.

Federal

Federal agencies like HHS and DoD engage with the private sector to **develop, test, approve, and produce** pathogen-specific diagnostics, vaccines, and treatments. They also test whether existing countermeasures for other diseases might be effective, assess current PPE stockpiles and take actions to prevent supply chain issues in the future.

Private Sector

Relevant companies in the private sector begin production of pathogen-specific **diagnostics, vaccines, and treatments.** Other companies integrate many data sources together to provide a map of the outbreak and its spread.

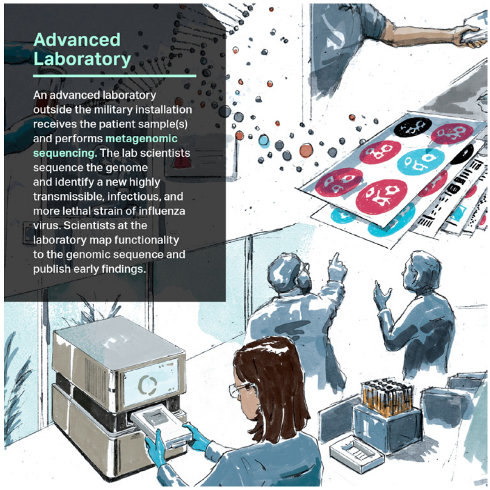
Military Installation

Using the genomic information for the new strain of influenza, the military installation initiates a quarantine of infected personnel, and assesses its operational capacity and readiness. The military installation also shifts its biosurveillance activities to more targeted detection approaches, such as:

1. **Increased antigen/PCR testing for influenza**
2. **Increased environmental detection (wastewater and air sampling)**
3. **Swabbing of high contact points within facilities**
4. **Increased serological testing**

Military Installation

After conducting **massively multiplexed testing**, the physician at the health clinic is unable to identify the pathogen/strain in question and sends the sample to a more advanced laboratory off base.



Advanced Laboratory

An advanced laboratory outside the military installation receives the patient sample(s) and performs **metagenomic sequencing**. The lab scientists sequence the genome and identify a new highly transmissible, infectious, and more lethal strain of influenza virus. Scientists at the laboratory map functionality to the genomic sequence and publish early findings.

Local + State Public Health

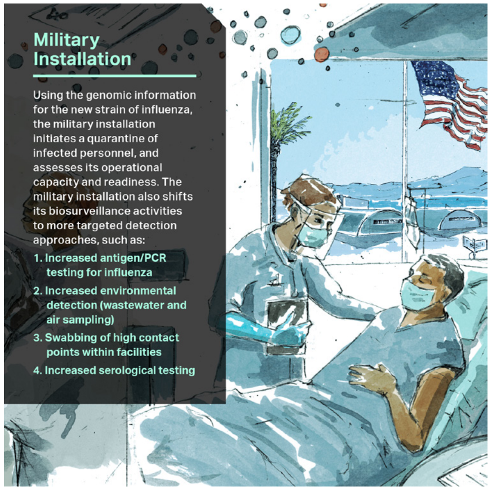
Local and state public health agencies report the case(s) to the CDC, initiate local epidemiological activities including contact tracing, and expand **biosurveillance** activities.

Federal

Federal agencies like HHS and DoD engage with the private sector to **develop, test, approve, and produce** pathogen-specific diagnostics, vaccines, and treatments. They also test whether existing countermeasures for other diseases might be effective, assess current PPE stockpiles and take actions to prevent supply chain issues in the future.

Private Sector

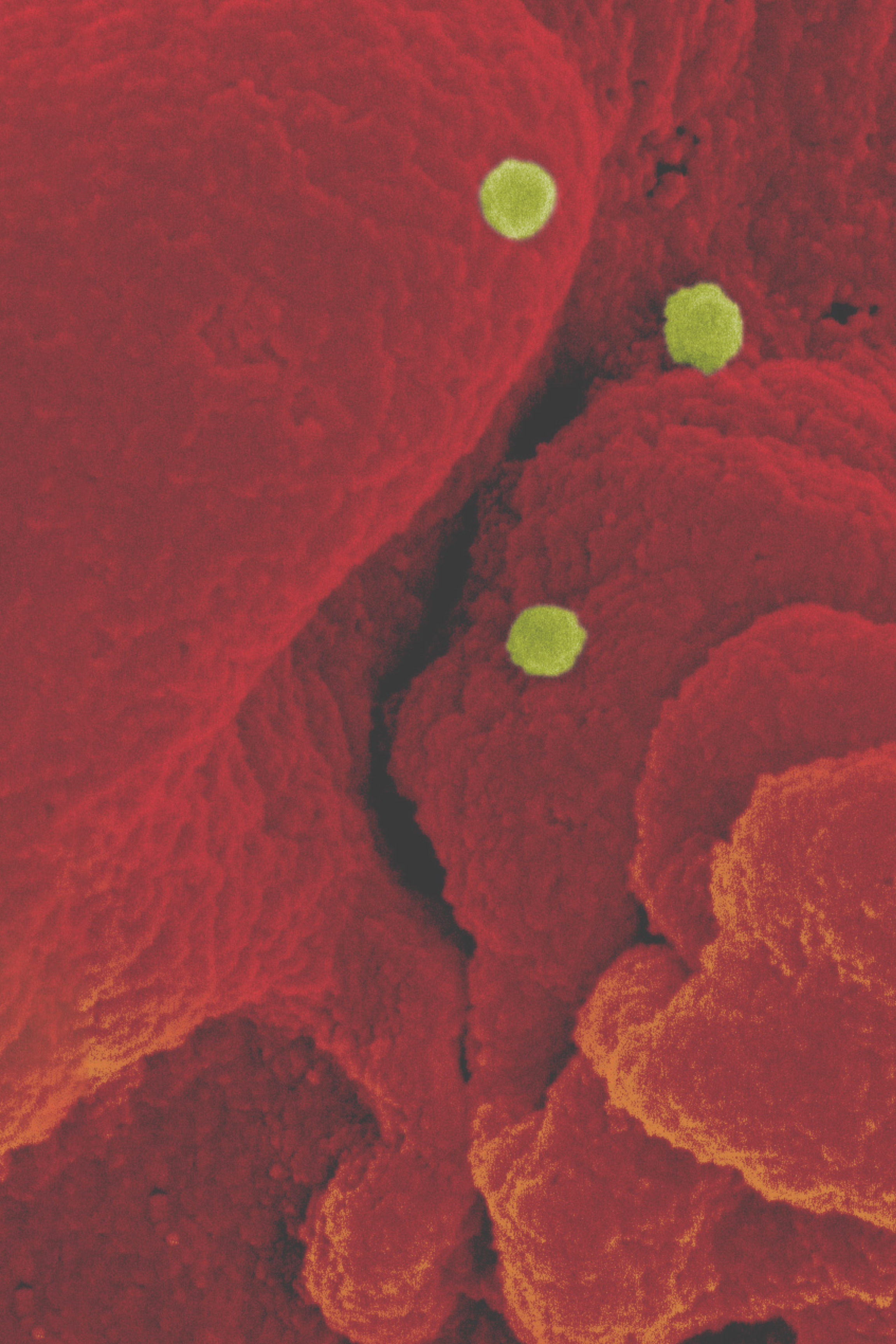
Relevant companies in the private sector begin production of pathogen-specific **diagnostics, vaccines, and treatments**. Other companies integrate many data sources together to provide a map of the outbreak and its spread.

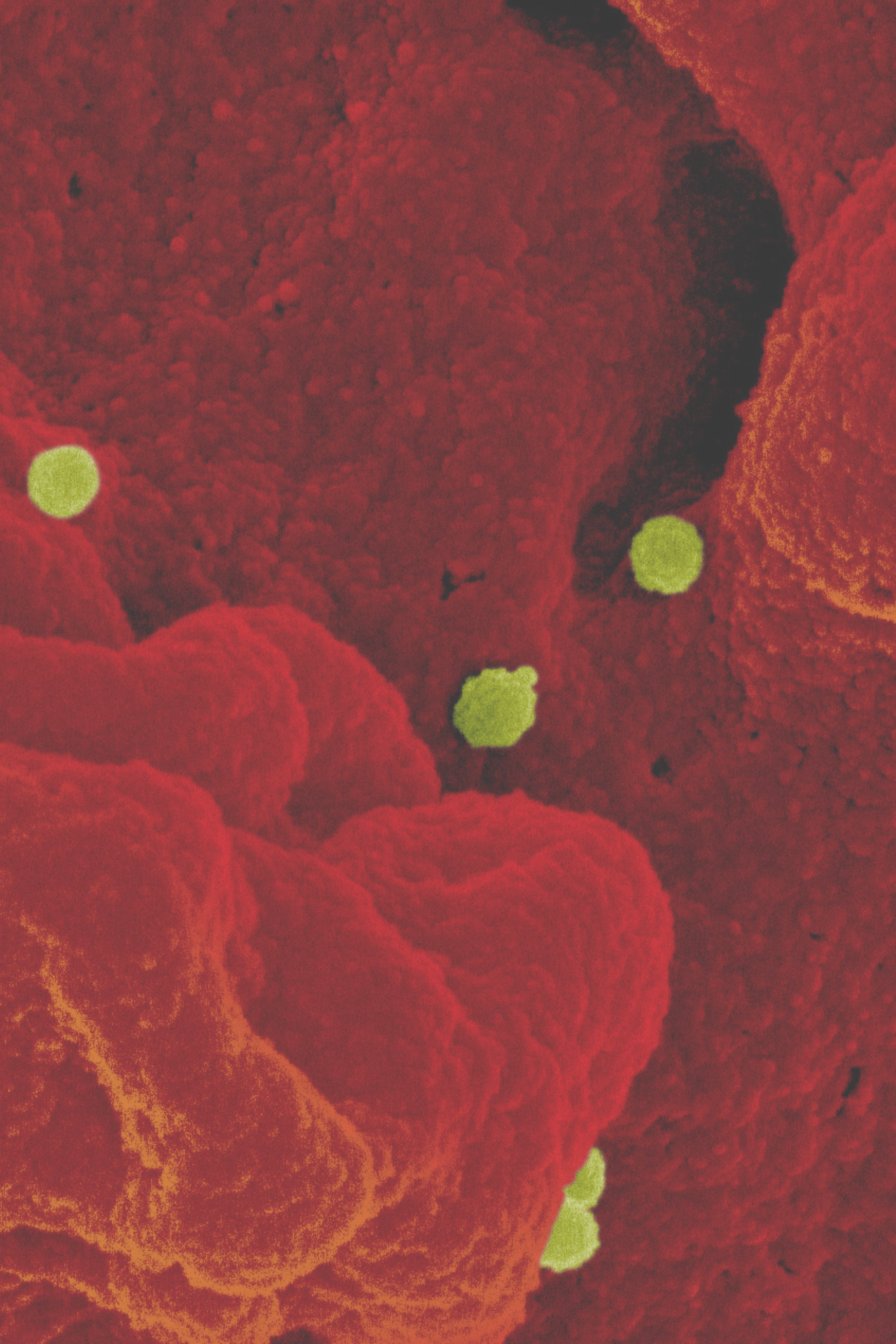


Military Installation

Using the genomic information for the new strain of influenza, the military installation initiates a quarantine of infected personnel, and assesses its operational capacity and readiness. The military installation also shifts its biosurveillance activities to more targeted detection approaches, such as:

1. **Increased antigen/PCR testing for influenza**
2. **Increased environmental detection (wastewater and air sampling)**
3. **Swabbing of high contact points within facilities**
4. **Increased serological testing**





COUNCIL ON STRATEGIC RISKS

The Janne E. Nolan Center on Strategic Weapons
an institute of The Council on Strategic Risks
www.councilonstrategicrisks.org

PRINTED IN THE UNITED STATES OF AMERICA